Integración del Metabolismo

II Semestre, 2025

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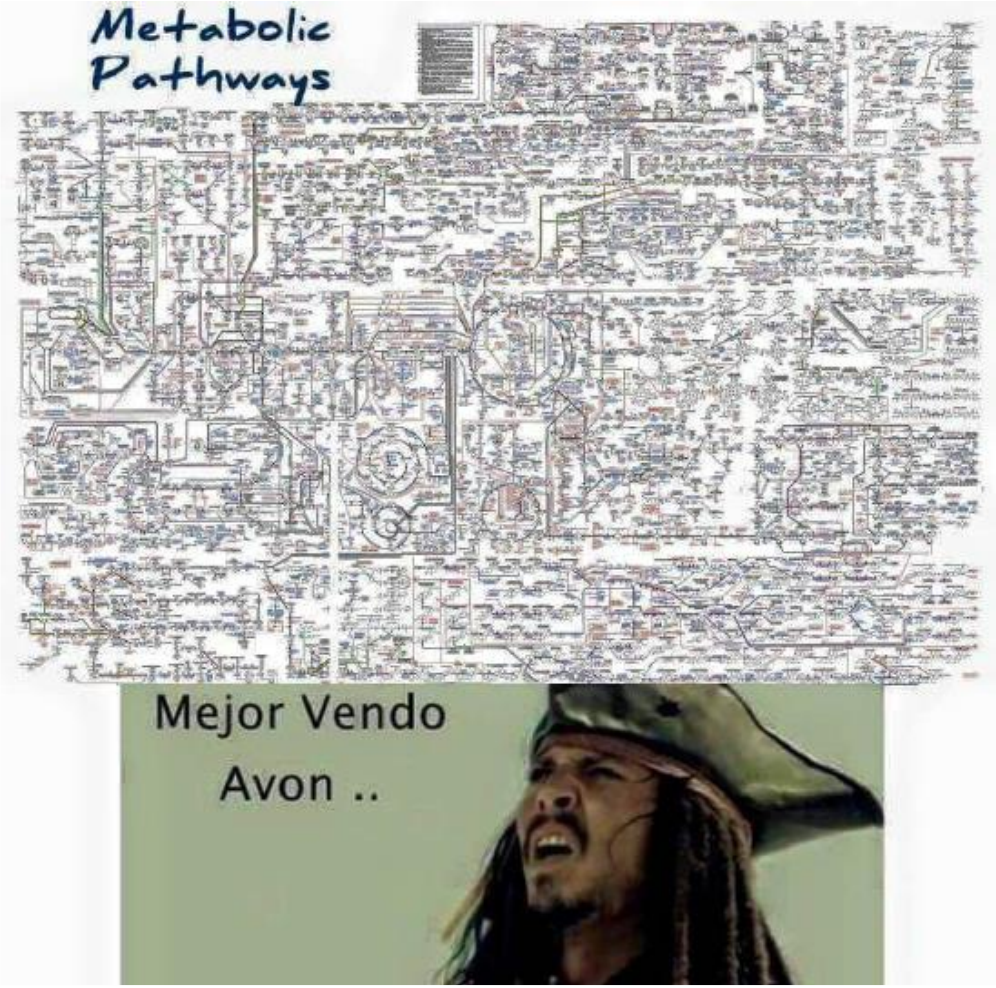
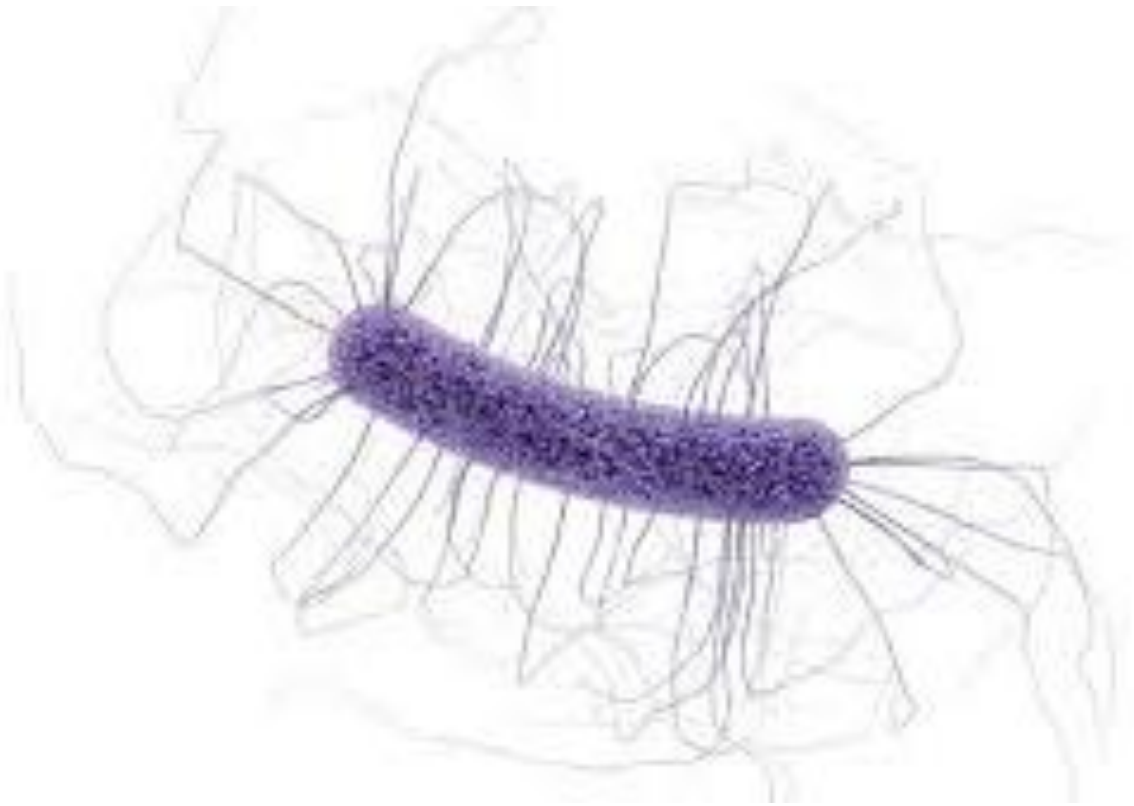
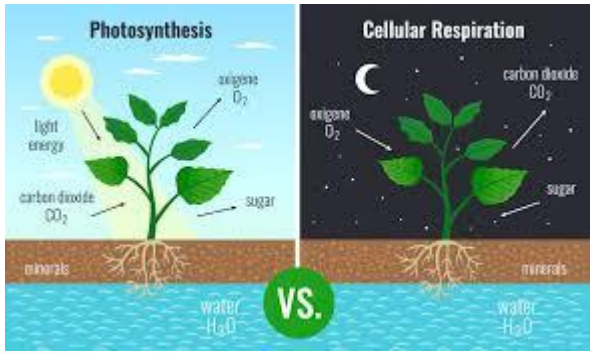
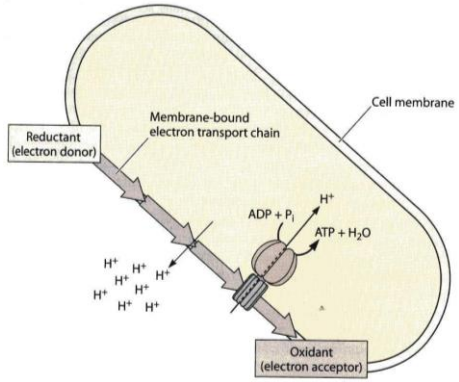
Pathway
Citric acid cycle: acetyl-CoA ⟶ $2CO_2$
Oxidative phosphorylation: ATP synthesis
Carbohydrate catabolism
Glycogenolysis: glycogen ⟶ glucose 1-phosphate ⟶ blood glucose
Hexose entry into glycolysis: fructose, mannose, galactose ⟶ glucose 6-phosphate
Glycolysis: glucose ⟶ pyruvate
Pyruvate dehydrogenase reaction: pyruvate ⟶ acetyl-CoA
Lactic acid fermentation: glycogen ⟶ lactate + 2ATP
Pentose phosphate pathway: glucose 6-phosphate ⟶ pentose phosphates + NADPH
Carbohydrate anabolism
Gluconeogenesis: citric acid cycle intermediates ⟶ glucose
Glucose-alanine cycle: glucose ⟶ pyruvate ⟶ alanine ⟶ glucose
Glycogen synthesis: glucose 6-phosphate ⟶ glucose 1-phosphate ⟶ glycogen
Amino acid and nucleotide metabolism
Amino acid degradation: amino acids ⟶ acetyl-CoA, citric acid cycle intermediates
Amino acid synthesis
Urea cycle: NH_3 ⟶ urea
Glucose-alanine cycle: alanine ⟶ glucose
Nucleotide synthesis: amino acids ⟶ purines, pyrimidines
Hormone and neurotransmitter synthesis
Fat catabolism
β Oxidation of fatty acids: fatty acid ⟶ acetyl-CoA
Oxidation of ketone bodies: β-hydroxybutyrate ⟶ acetyl-CoA ⟶ CO_2
Fat anabolism
Fatty acid synthesis: acetyl-CoA ⟶ fatty acids
Triacylglycerol synthesis: acetyl-CoA ⟶ fatty acids ⟶ triacylglycerol
Ketone body formation: acetyl-CoA ⟶ acetoacetate, β-hydroxybutyrate
Cholesterol and cholesteryl ester synthesis: acetyl-CoA ⟶ cholesterol ⟶ cholesteryl esters
Phospholipid synthesis: fatty acids ⟶ phospholipids









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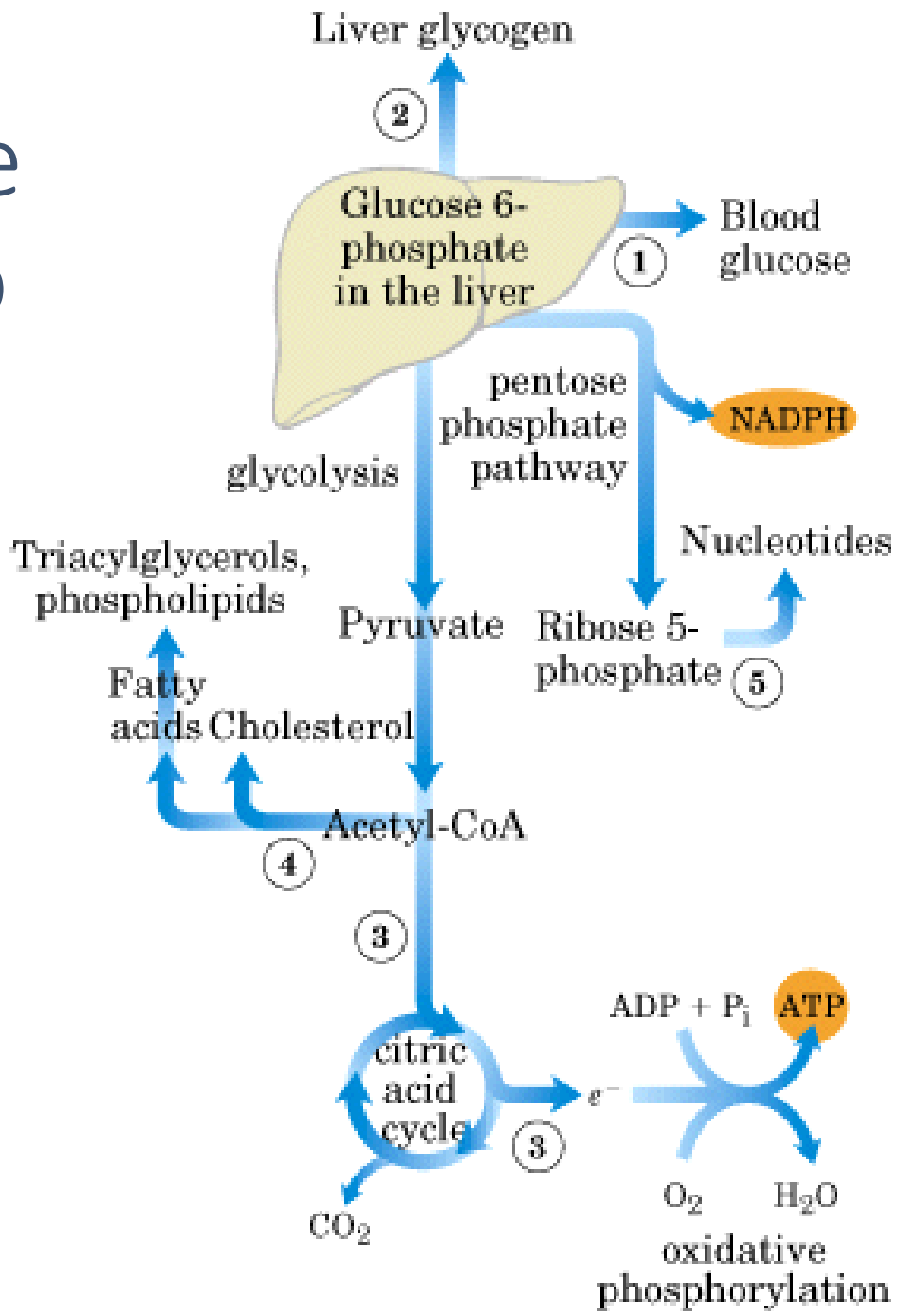
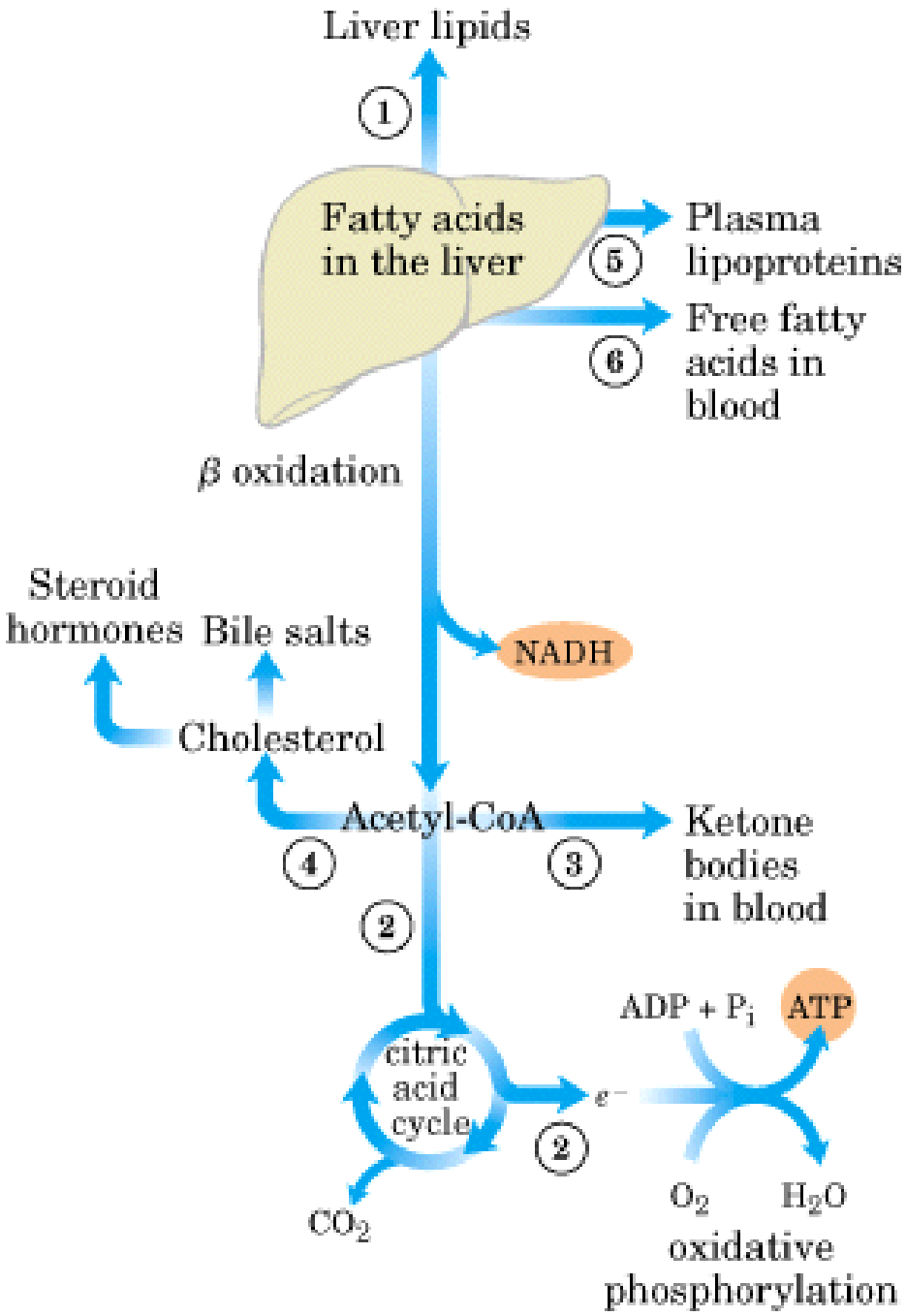
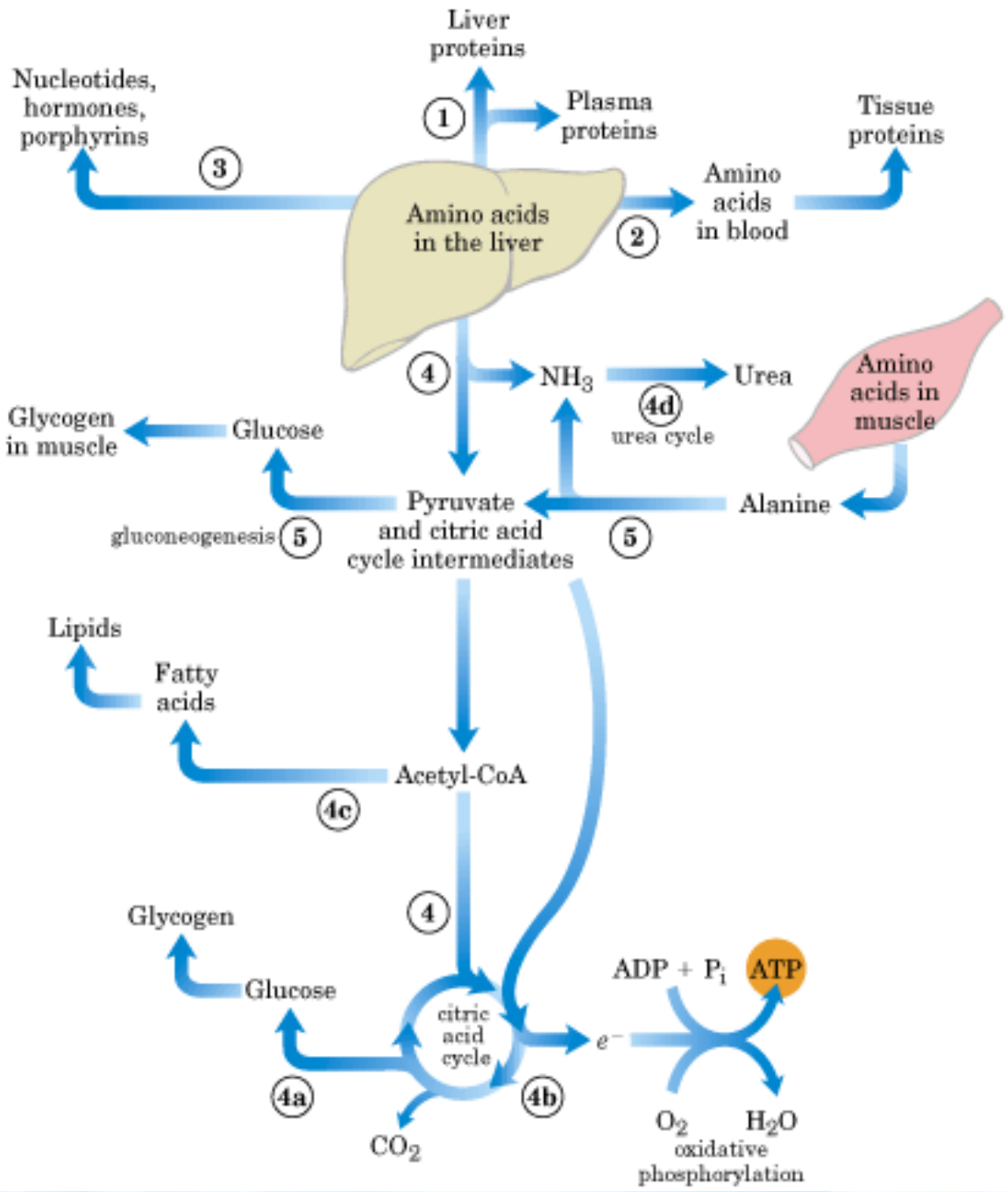
Vías metabólicas de la glucosa-6-fosfato en el hígado



Metabolismo de ácidos grasos en el hígado



Metabolismo de aminoácidos en el hígado



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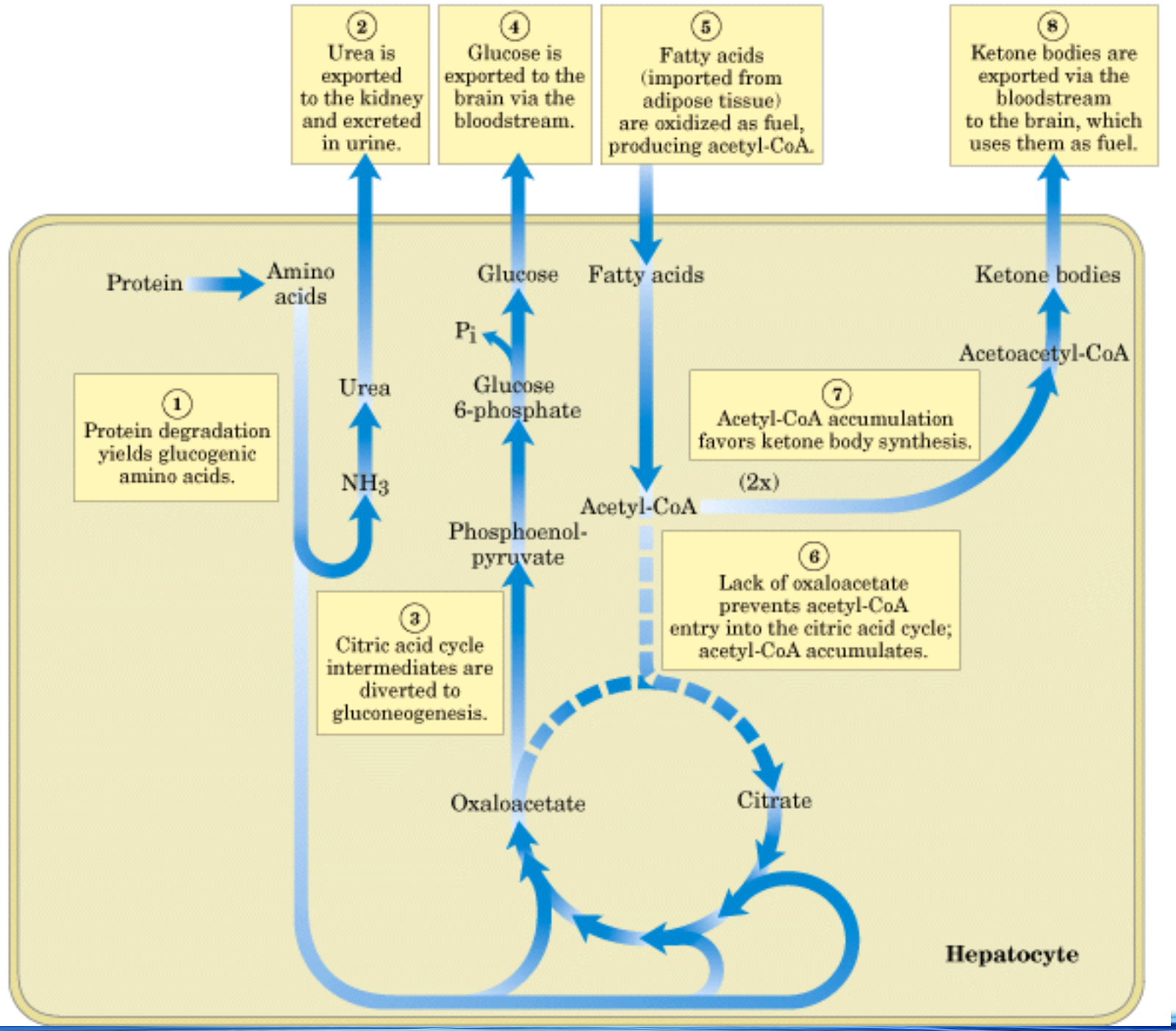
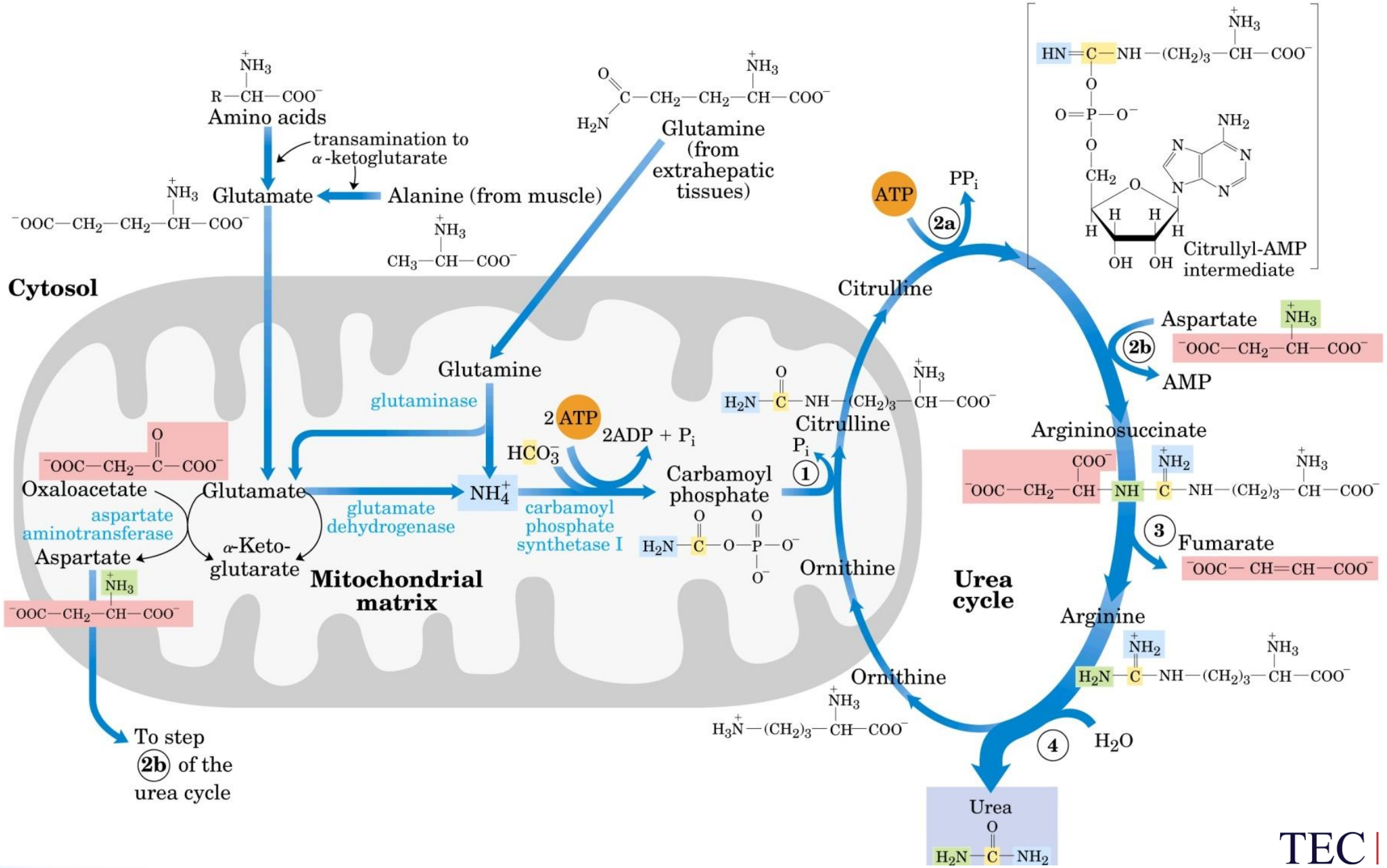
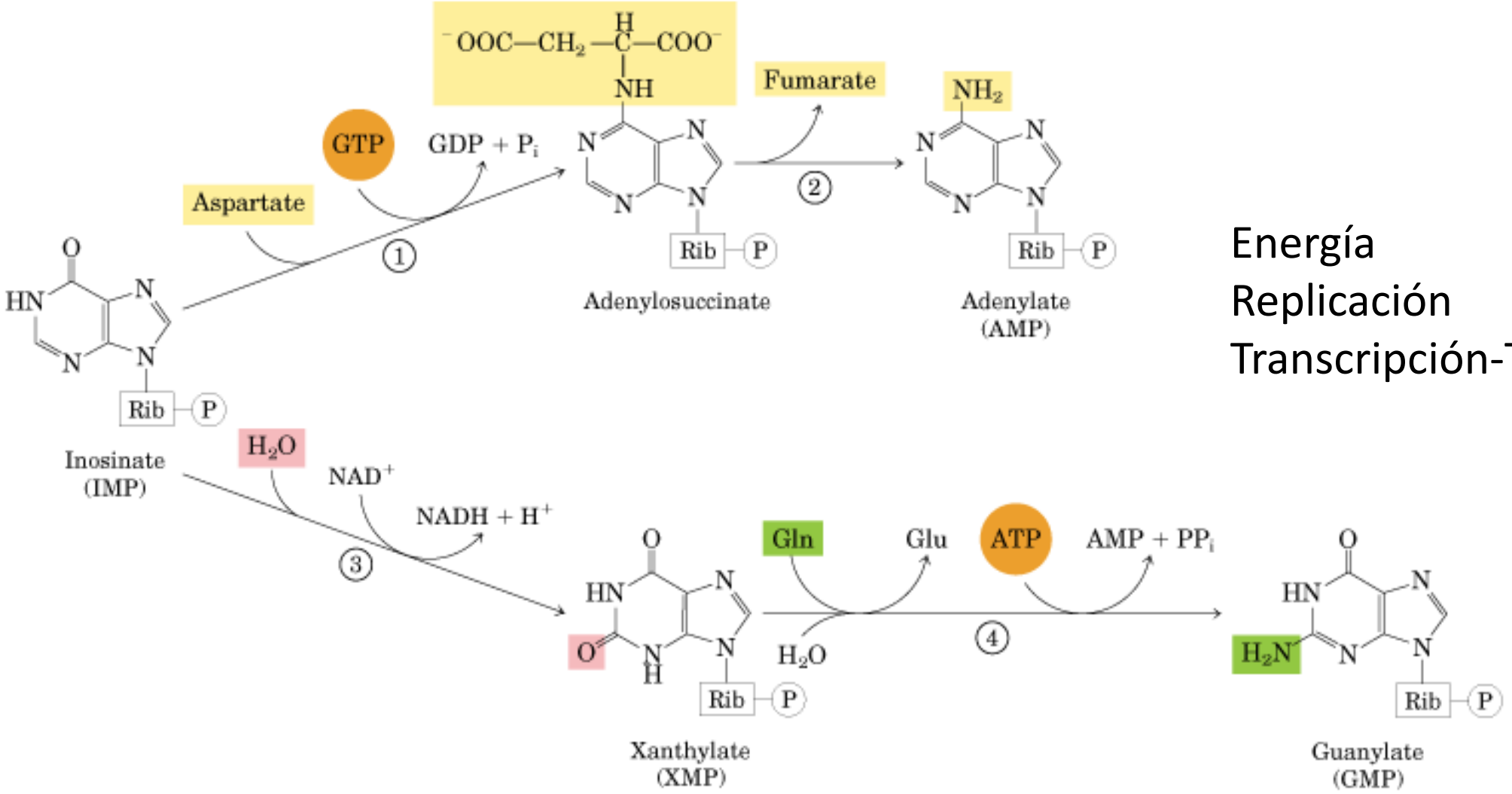

2 Urea is exported to the kidney and excreted in urine.
4 Glucose is exported to the brain via the bloodstream.
5 Fatty acids (imported from adipose tissue) are oxidized as fuel, producing acetyl-CoA.
8 Ketone bodies are exported via the bloodstream to the brain, which uses them as fuel.
Protein
Amino acids
Glucose
Fatty acids
Ketone bodies
Pi
Acetoacetyl-CoA
Urea
Glucose 6-phosphate
1 Protein degradation yields glucogenic amino acids.
7 Acetyl-CoA accumulation favors ketone body synthesis.
NH3
(2x)
Acetyl-CoA
Phosphoenol-pyruvate
6 Lack of oxaloacetate prevents acetyl-CoA entry into the citric acid cycle; acetyl-CoA accumulates.
3 Citric acid cycle intermediates are diverted to gluconeogenesis.
Oxaloacetate
Citrate
Hepatocyte

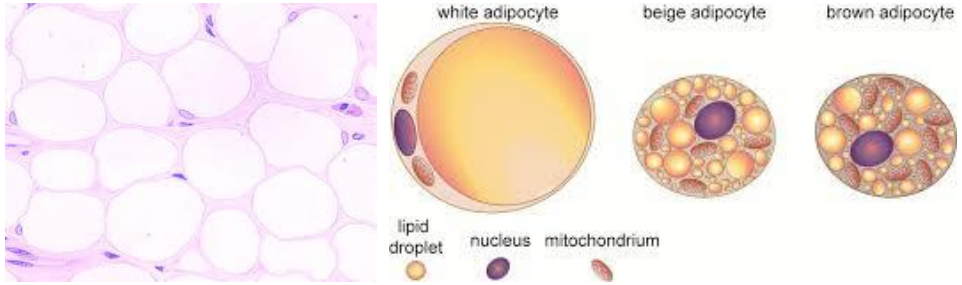

Amino acids
transamination to α-ketoglutarate
Glutamate
Alanine (from muscle)
Glutamine (from extrahepatic tissues)
Cytosol
Glutamine
glutaminase
2 ATP
2ADP + Pi
HCO3−
Carbamoyl phosphate
carbamoyl phosphate synthetase I
Oxaloacetate
Glutamate
glutamate dehydrogenase
NH4+
aspartate aminotransferase
Aspartate
α-Keto-glutarate
Mitochondrial matrix
To step 2b of the urea cycle
Citrulline
Pi
1
Ornithine
ATP
PPi
2a
Citrullyl-AMP intermediate
Aspartate
2b
AMP
Argininosuccinate
3
Fumarate
Urea cycle
Arginine
Ornithine
4
H2O
Urea

Síntesis de AMP y GMP a partir de IMP

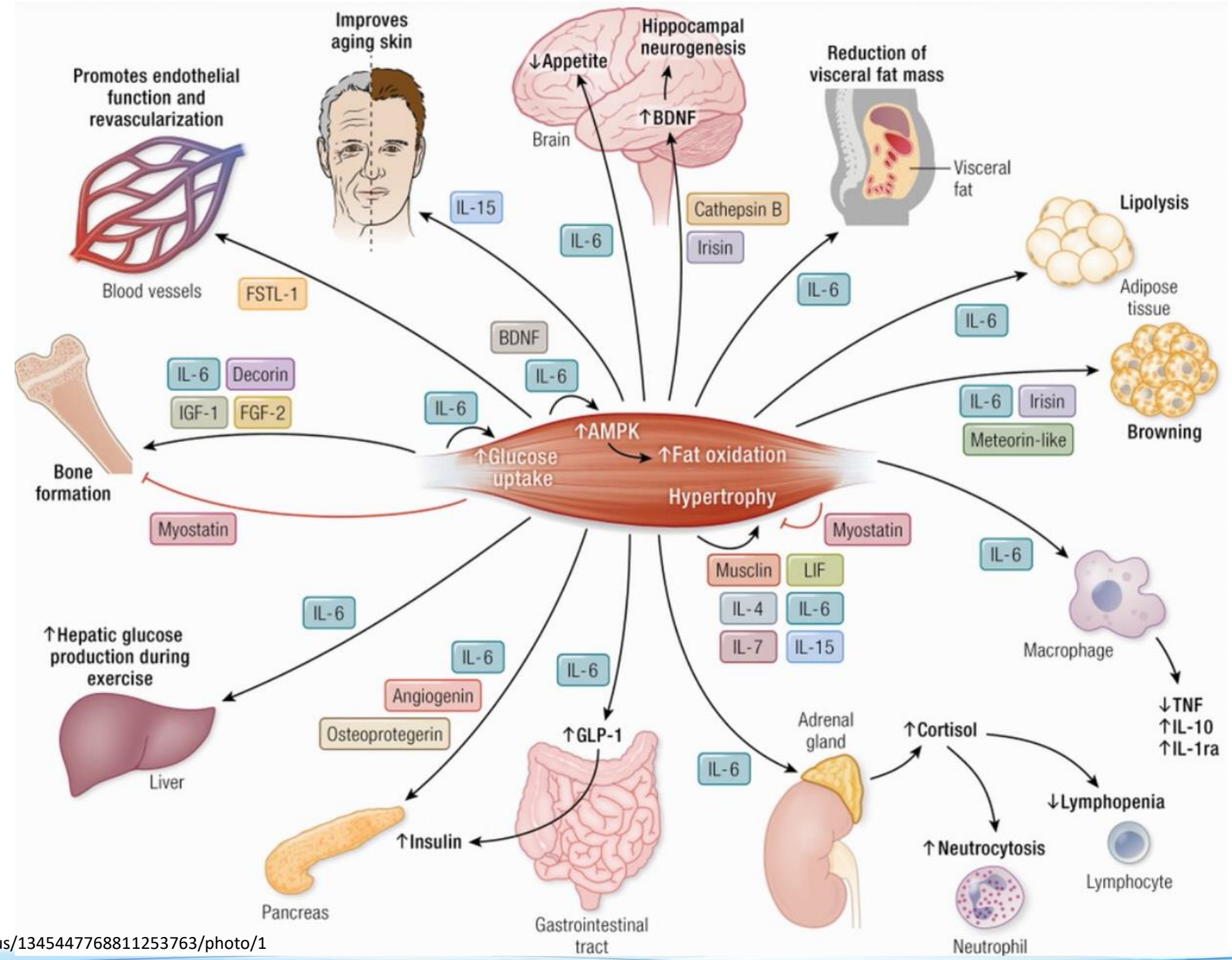


Energía
Replicación
Transcripción-Traducción

Metabolismo en los adipocitos



- Tejido amorfo y ampliamente distribuido
- 65% de su masa son triglicéridos
- Metabólicamente “muy activo”, responde a estímulos hormonales y libera hormonas
  - Metabolismo glicolítico, usa el ciclo de Krebs para oxidar piruvato y ácidos grasos, realiza fosforilación oxidativa
  - Convierte glucosa en ácidos grasos que se usan en la síntesis de triglicéridos (hígado)
  - Por acción de lipasas libera ácidos grasos
  - Tejido graso pardo



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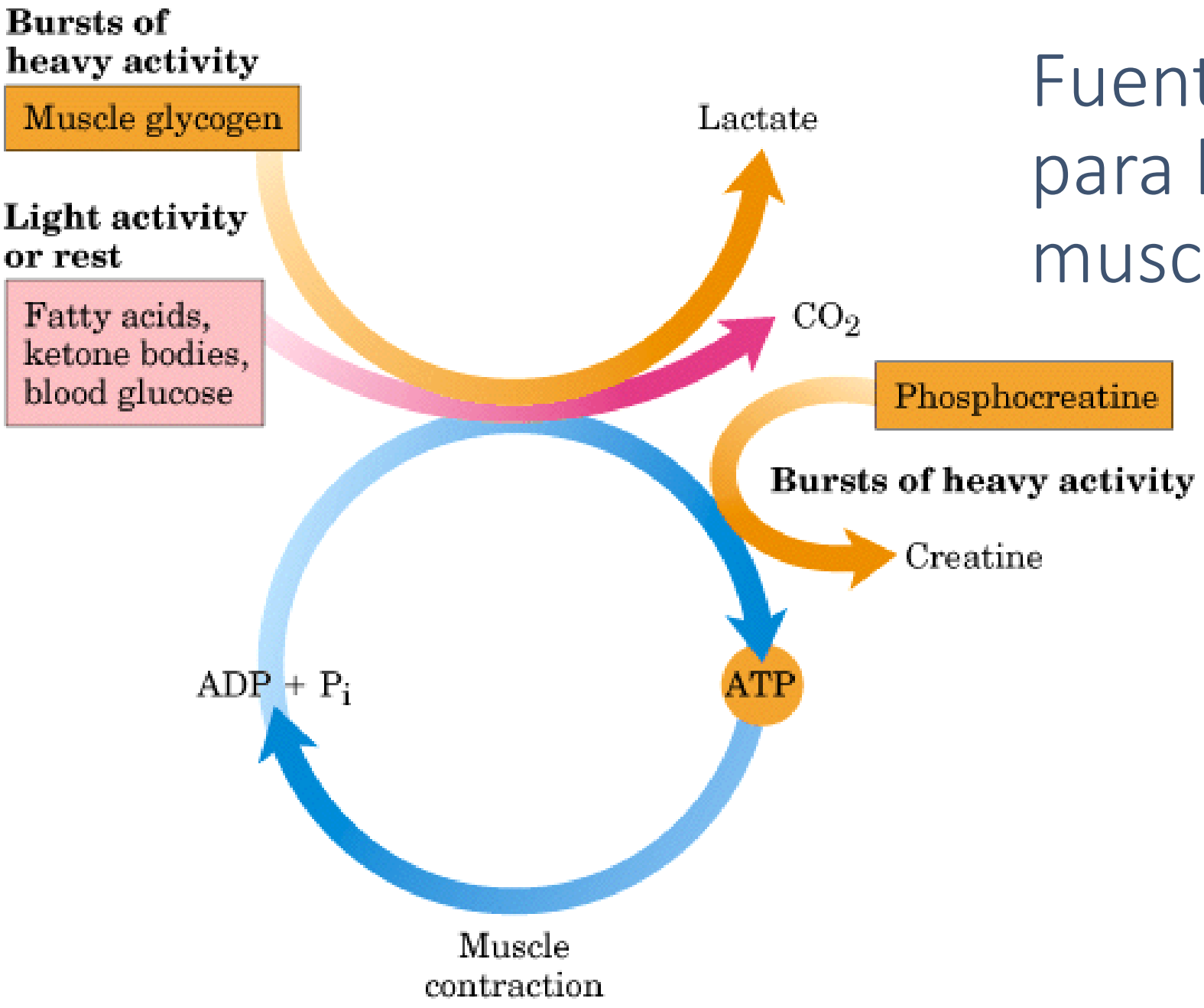
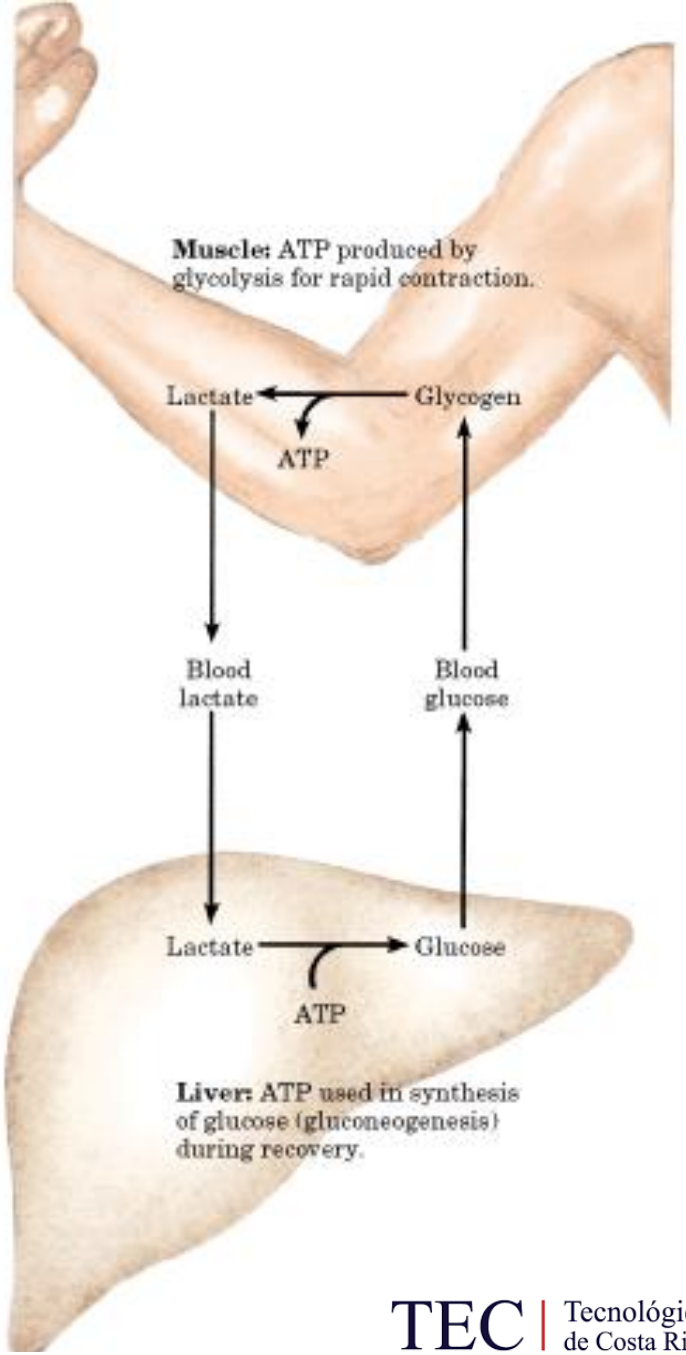
Fuentes de energía para la contracción muscular



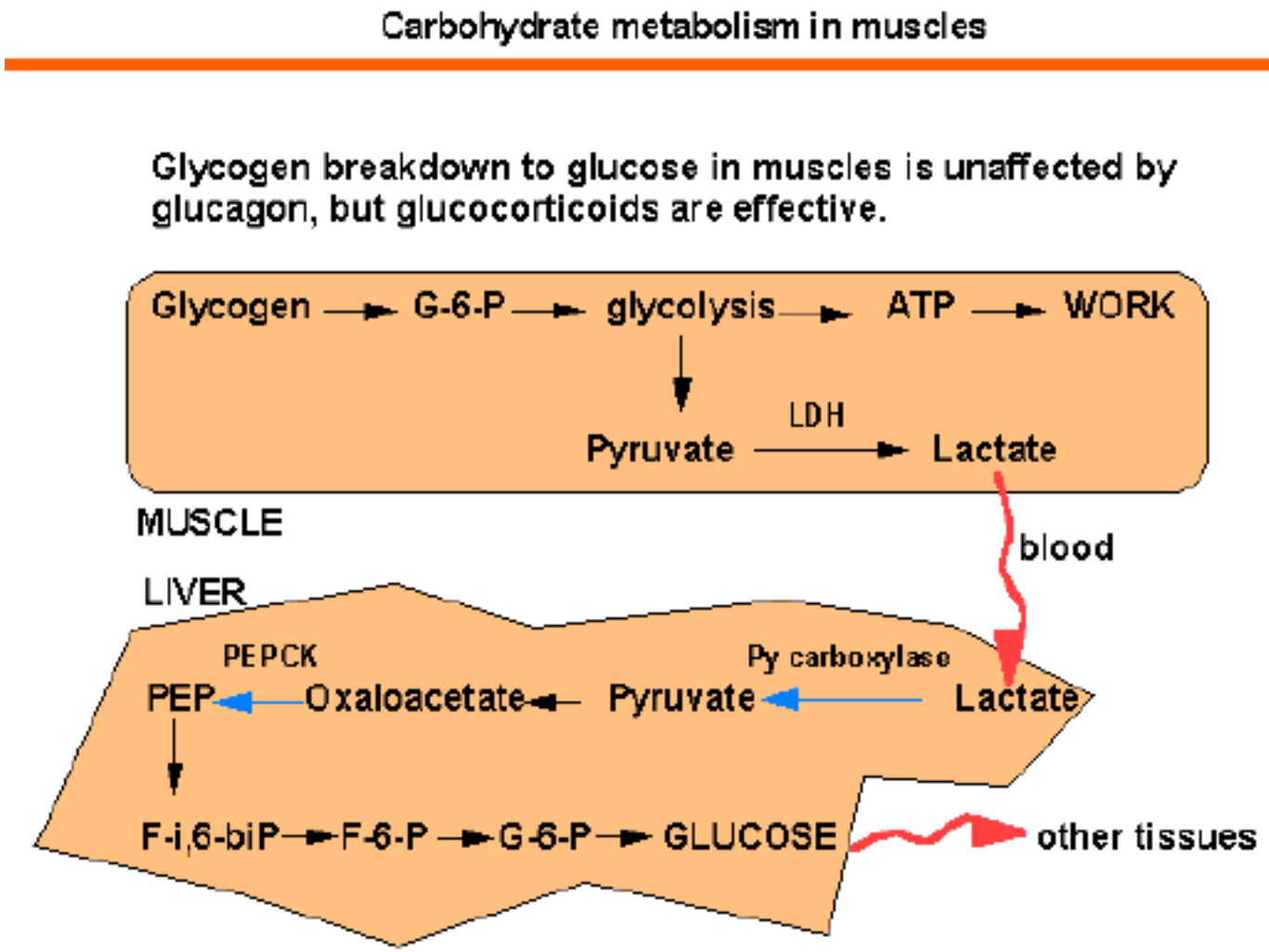
Ejemplo de cooperación metabólica entre el músculo esquelético y el hígado

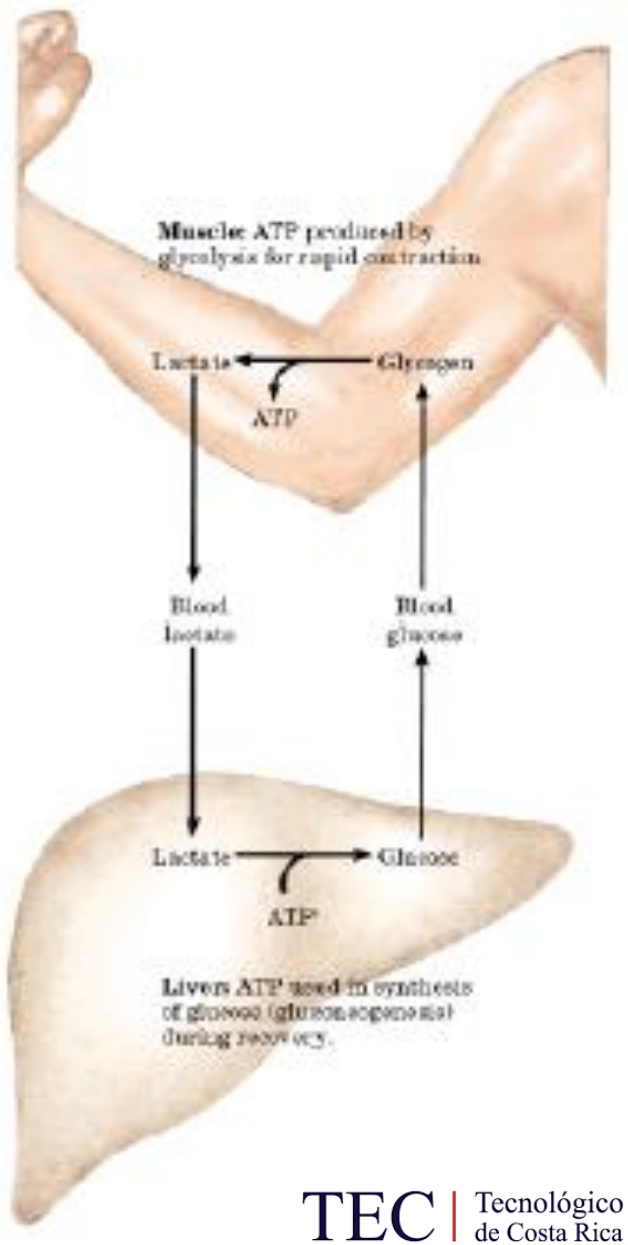
- La acumulación de lactato y la disminución del pH disminuyen su eficiencia

- Luego de un periodo de actividad intensa la respiración profunda continúa para la fosforilación oxidativa y producción de ATP usado en gluconeogénesis a partir de lactato

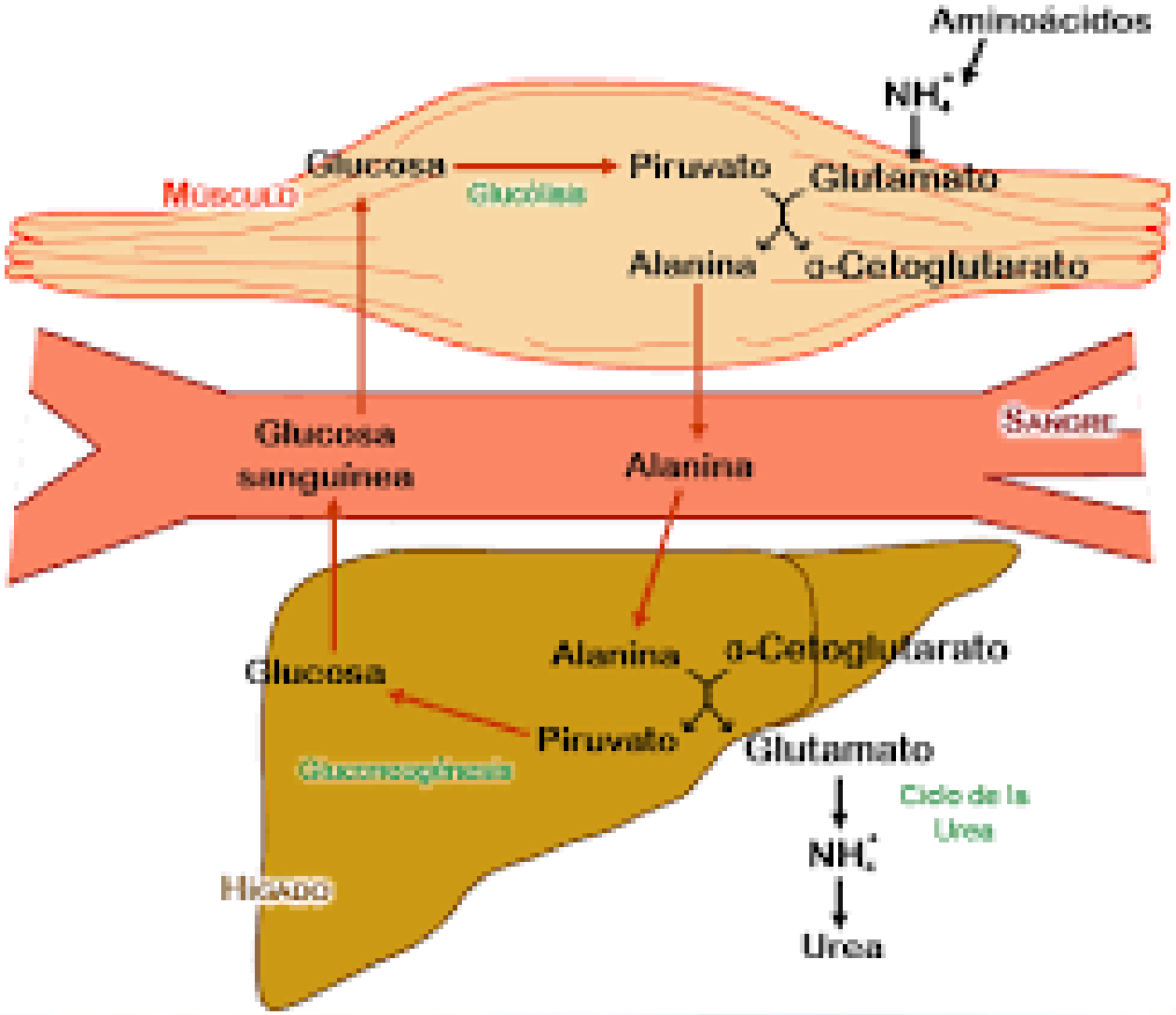


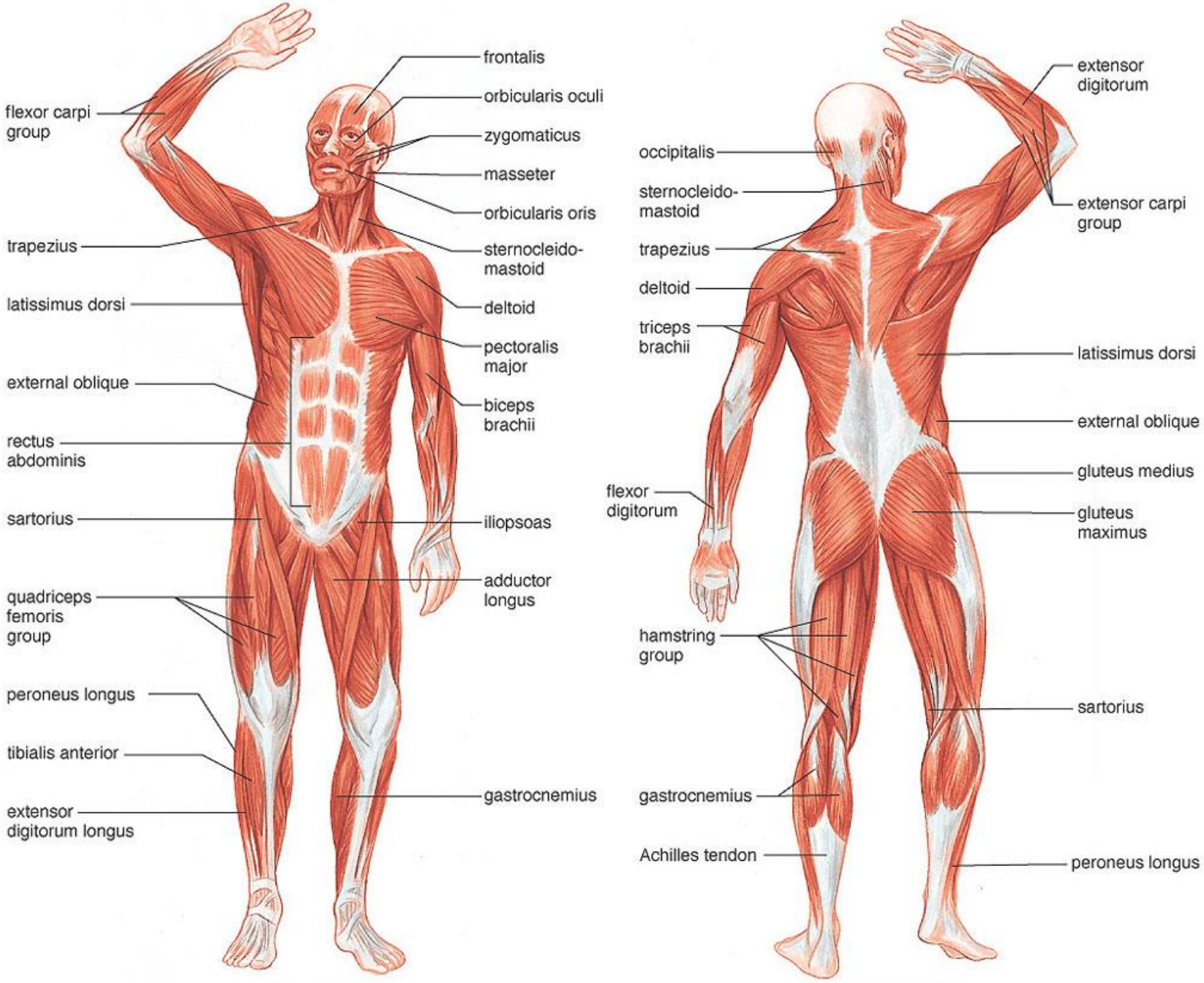
Ciclo de Cori o del ácido láctico





Ciclo de la glucosa-alanina

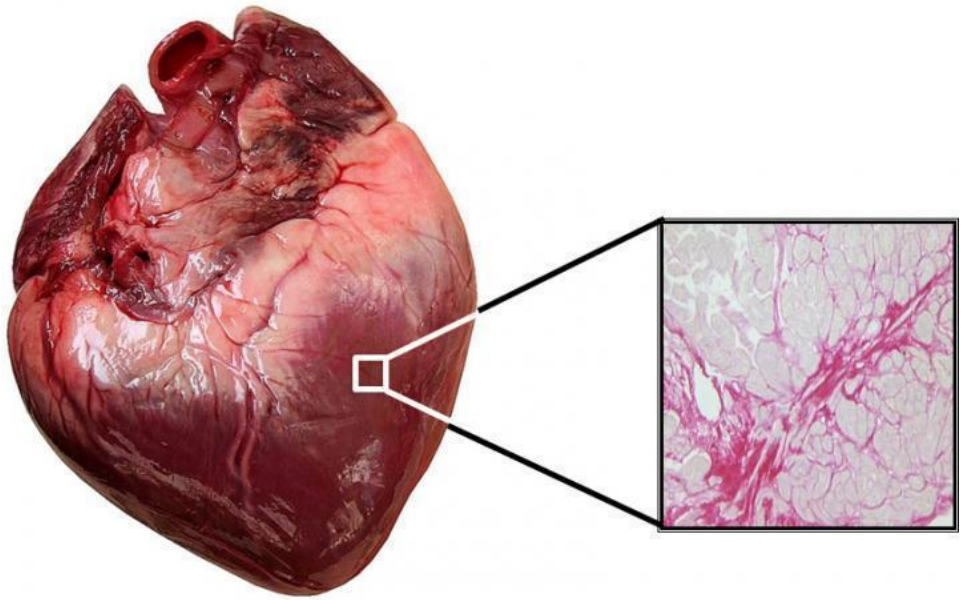




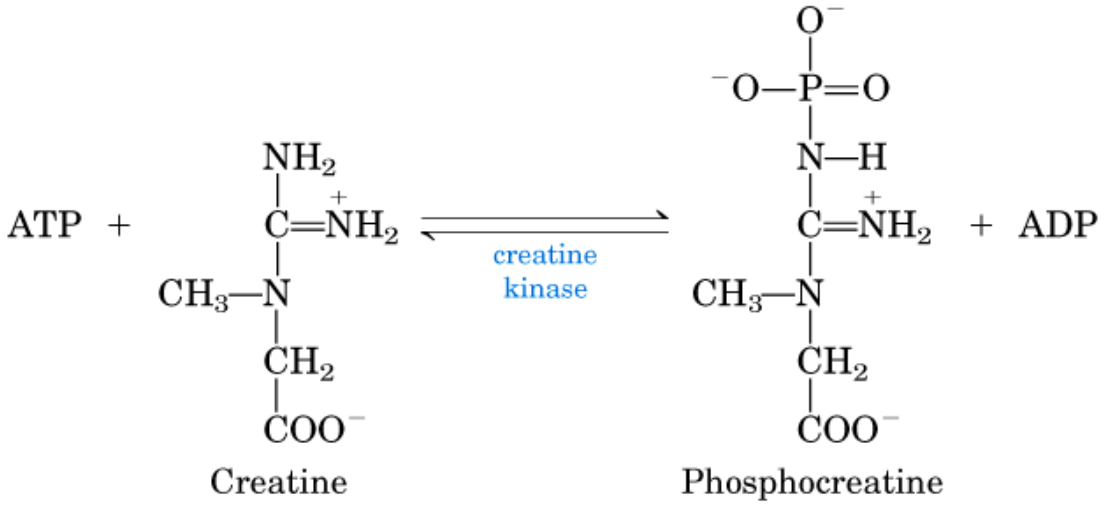
a. Anterior view

b. Posterior view

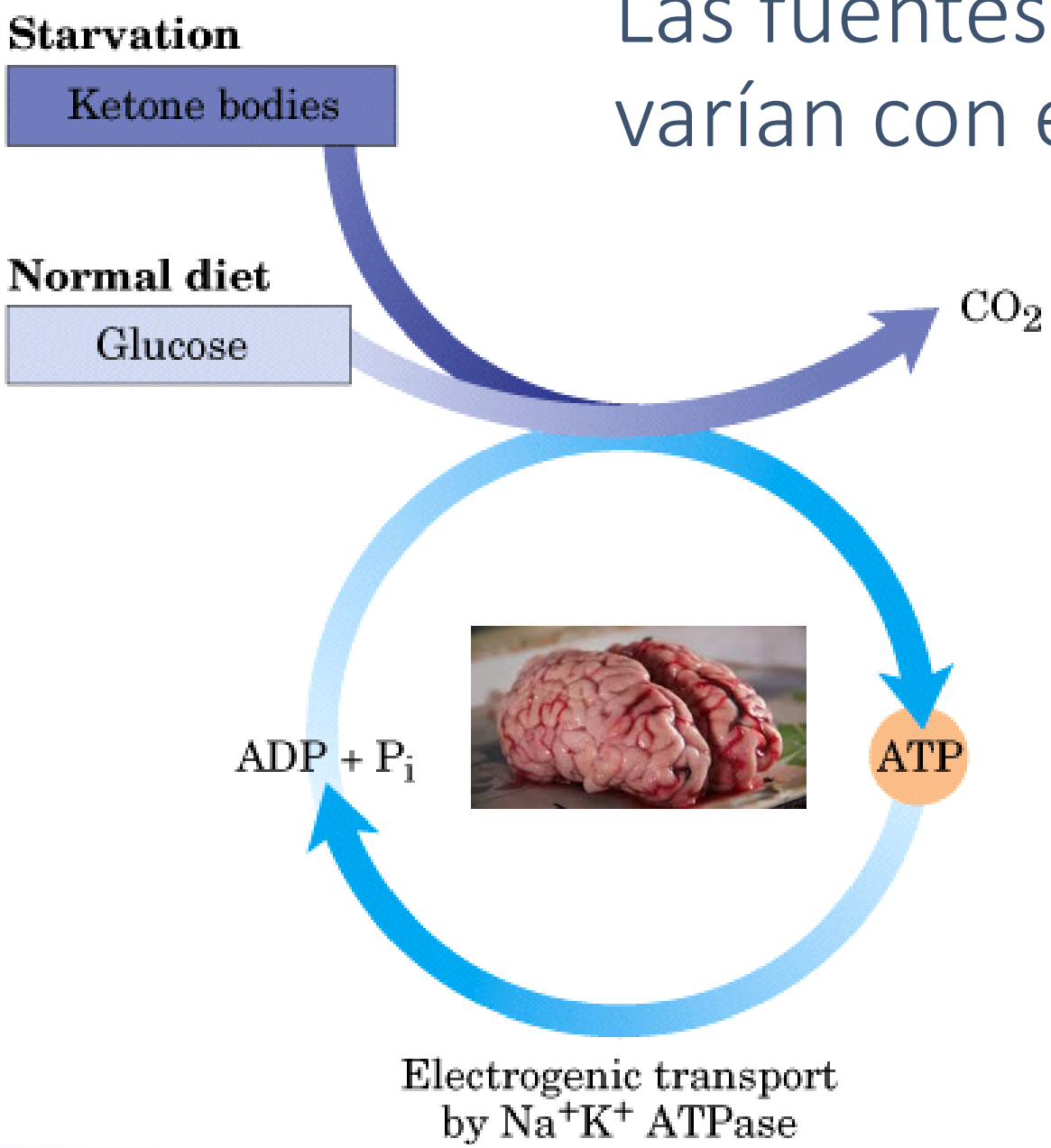
En el corazón

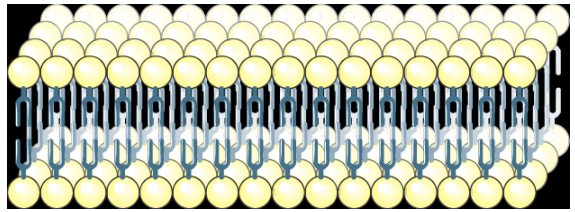


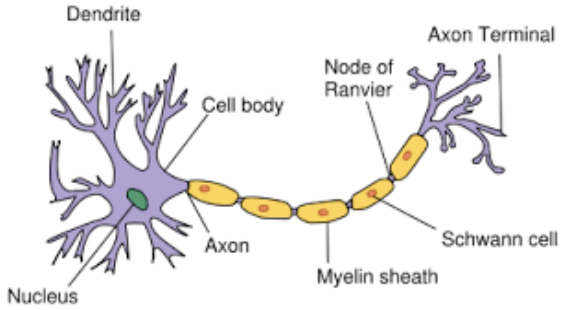
- Actividad muscular continua y rítmica
- Metabolismo aeróbico
  - Pequeñas cantidades de glucógeno y fosfocreatina

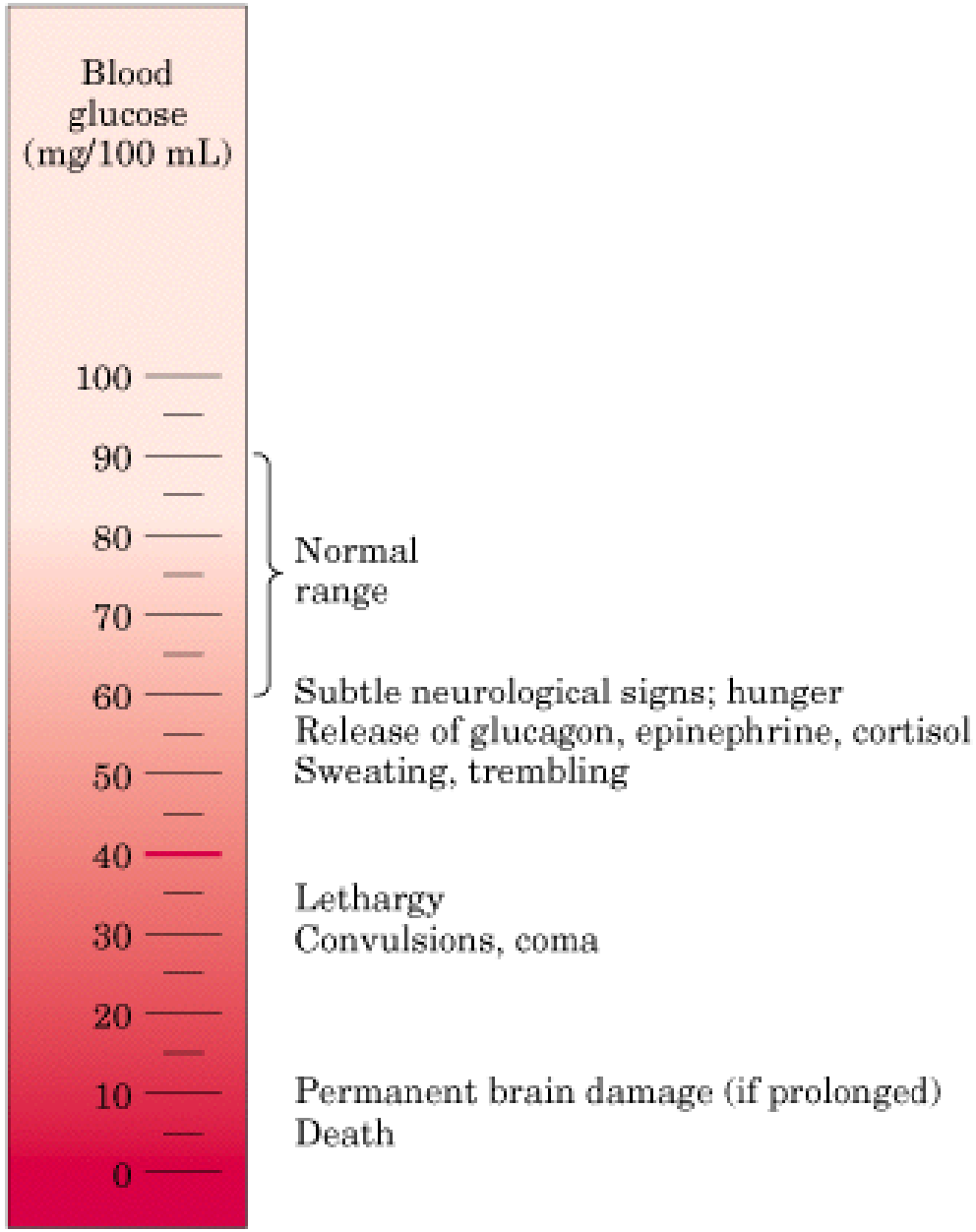


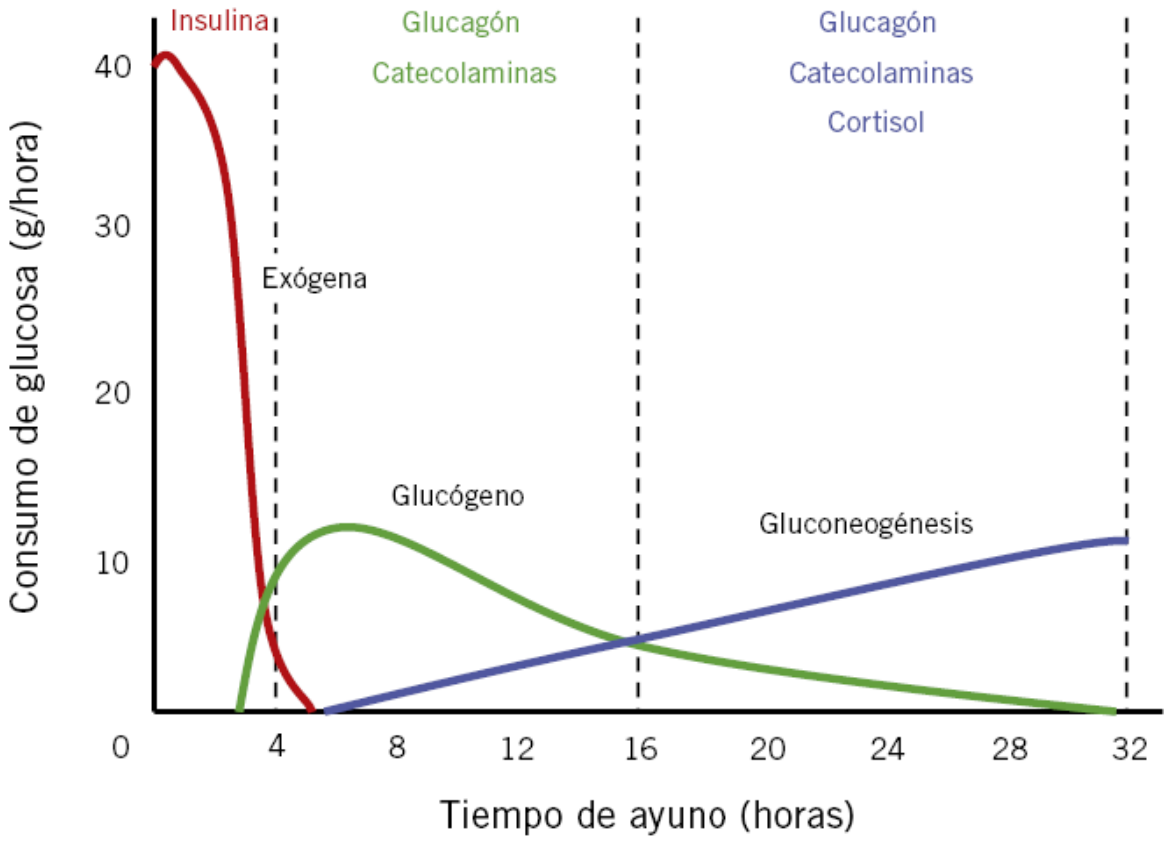
Las fuentes energéticas en el cerebro varían con el estado nutricional








Blood glucose (mg/100 mL)
100
90
80
70
60
50
40
30
20
10
0
Normal range
Subtle neurological signs; hunger
Release of glucagon, epinephrine, cortisol
Sweating, trembling
Lethargy
Convulsions, coma
Permanent brain damage (if prolonged)
Death


Insulina
Glucagón
Catecolaminas
Glucagón
Catecolaminas
Cortisol
Exógena
Glucógeno
Gluconeogénesis
Consumo de glucosa (g/hora)
40
30
20
10
0
4
8
12
16
20
24
28
32
Tiempo de ayuno (horas)

Regulación hormonal de los combustibles metabólicos

FIGHT or FLIGHT

STRESS

Fight
Flight
Freeze

Epinefrina (AMPc)

Physiological and Metabolic Effects of Epinephrine: Preparation for Action

Physiological

- ↑ Heart rate
- ↑ Blood pressure
- ↑ Dilation of respiratory passages

} Increased delivery of O_2 to tissues (muscle)

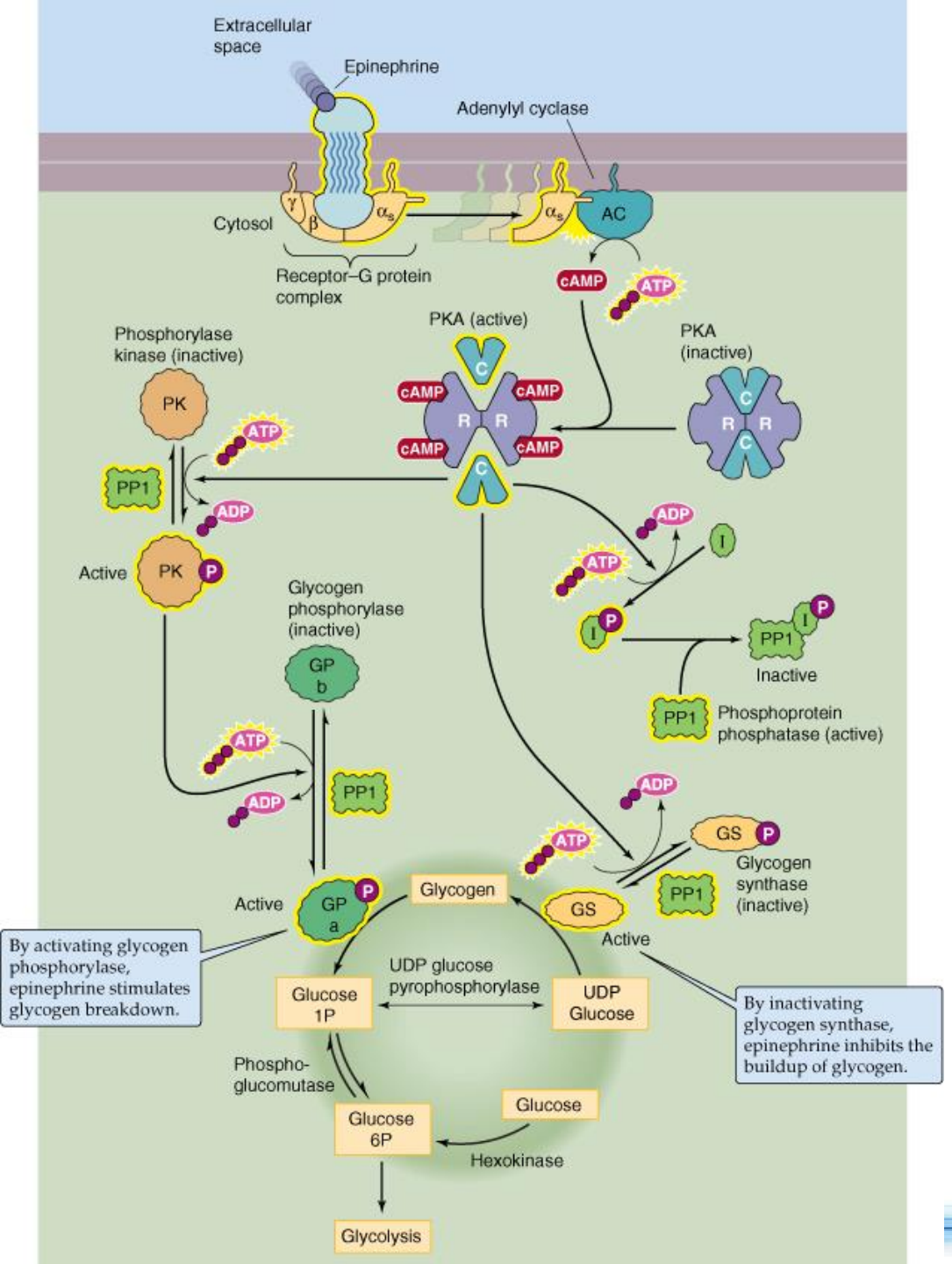
Metabolic

- ↑ Glycogen breakdown (muscle, liver)
- ↓ Glycogen synthesis (muscle, liver)
- ↑ Gluconeogenesis (liver)

} Increased production of glucose for fuel

- ↑ Glycolysis (muscle) ↑ **Fru-2,6-BP** — Increased ATP production in muscle
- ↑ Fatty acid mobilization (adipose tissue) — Increased availability of fatty acids as fuel
- ↑ Glucagon secretion
- ↓ Insulin secretion

} Reinforce metabolic effects of epinephrine



- cAMP realiza su efecto incrementando la acción de la protein-quinasa A (PKA)
- La epinefrina estimula la degradación e inhibe la síntesis de glucógeno vía cAMP
- Las fosfatasas revierten el efecto de las kinasas

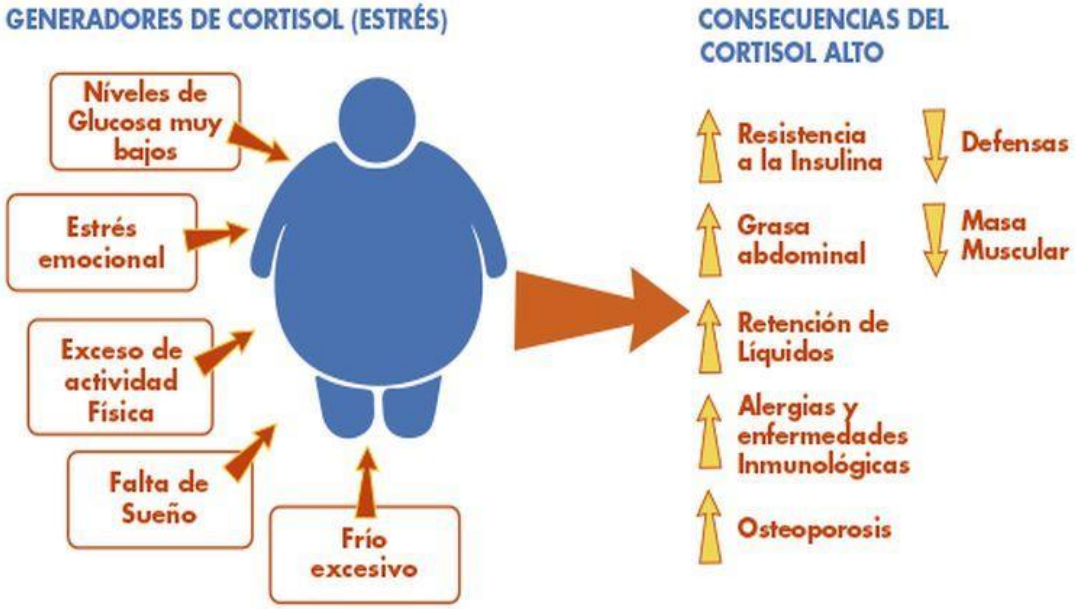
Glucagón (AMPc)

Effects of Glucagon on Blood Glucose: Production and Release of Glucose By the Liver

Metabolic effect	Effect on glucose metabolism	Target enzyme
↑ Glycogen breakdown (liver)	Glycogen ⟶ glucose	↑ Glycogen phosphorylase
↓ Glycogen synthesis (liver)	Less glucose stored as glycogen	↓ Glycogen synthase
↓ Glycolysis (liver)	Less glucose used as fuel in liver	↓ Phosphofructokinase-1
↑ Gluconeogenesis (liver)	Amino acids, Glycerol, Oxaloacetate ⟶ glucose	↑ Fructose 1,6-bisphosphatase ↓ Pyruvate kinase
↑ Fatty acid mobilization (adipose tissue)	Less glucose used as fuel by liver, muscle	↑ Triacylglycerol lipase

Cortisol

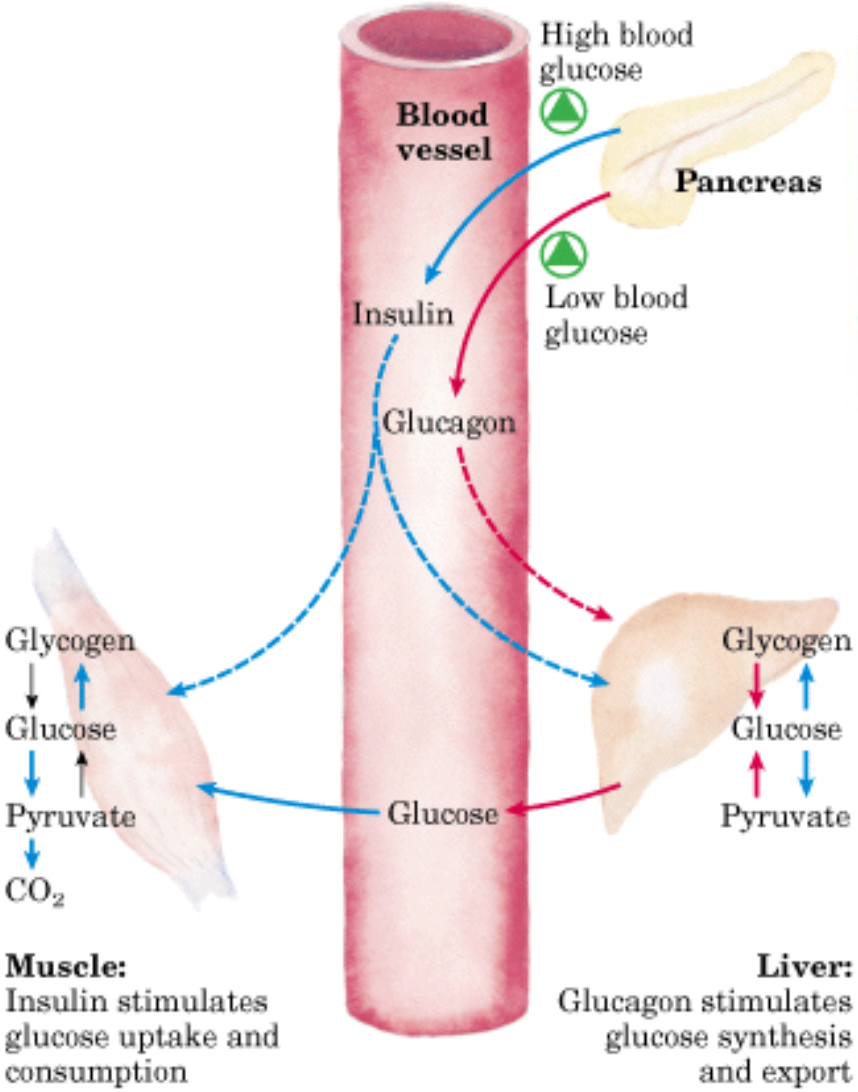
- Diferentes tipos de estrés: ansiedad, temor, dolor, hemorragia, infecciones, hipoglicemia
- Efecto lento: regula la cantidad y tipo de las enzimas nuevas
- Estimula la degradación de proteínas no esenciales y el transporte de aminoácidos al hígado

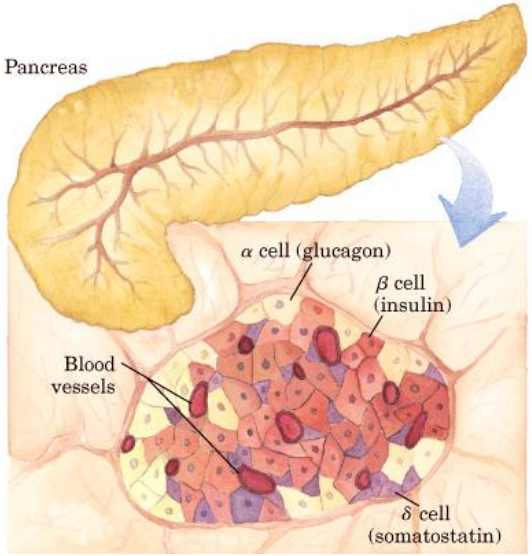


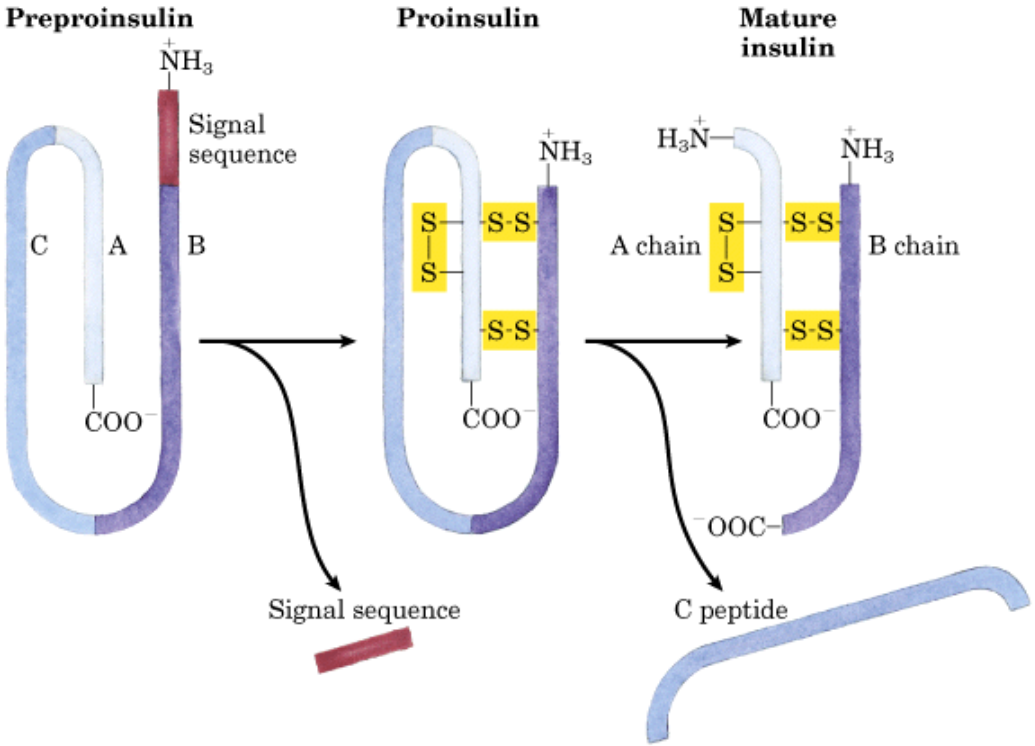
Insulina

Effect of Insulin on Blood Glucose: Uptake of Glucose by Cells and Storage as Triacylglycerols and Glycogen

Metabolic effect	Target enzyme
↑ Glucose uptake (muscle)	↑ Glucose transporter
↑ Glucose uptake (liver)	↑ Glucokinase
↑ Glycogen synthesis (liver, muscle)	↑ Glycogen synthase
↓ Glycogen breakdown (liver, muscle)	↓ Glycogen phosphorylase
↑ Glycolysis, acetyl-CoA production (liver, muscle)	↑ Phosphofructokinase-1
	↑ Pyruvate dehydrogenase complex
↑ Fatty acid synthesis (liver)	↑ Acetyl-CoA carboxylase
↑ Triacylglycerol synthesis (adipose tissue)	↑ Lipoprotein lipase

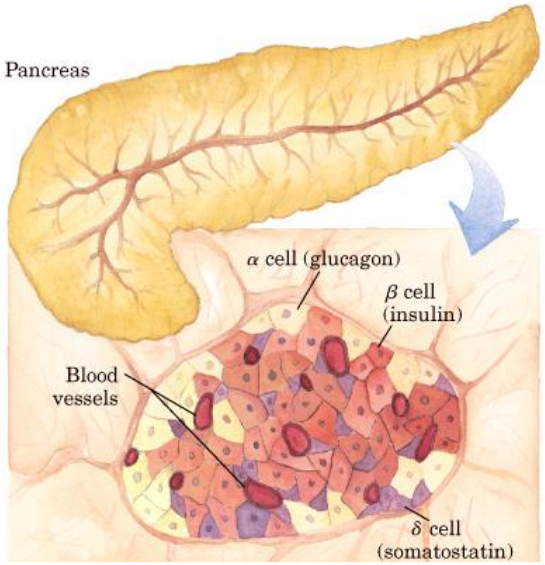

High blood glucose
Blood vessel
Pancreas
Insulin
Low blood glucose
Glucagon
Glycogen
Glucose
Pyruvate
CO_2
Glucose
Glycogen
Glucose
Pyruvate
Muscle:
Insulin stimulates glucose uptake and consumption
Liver:
Glucagon stimulates glucose synthesis and export

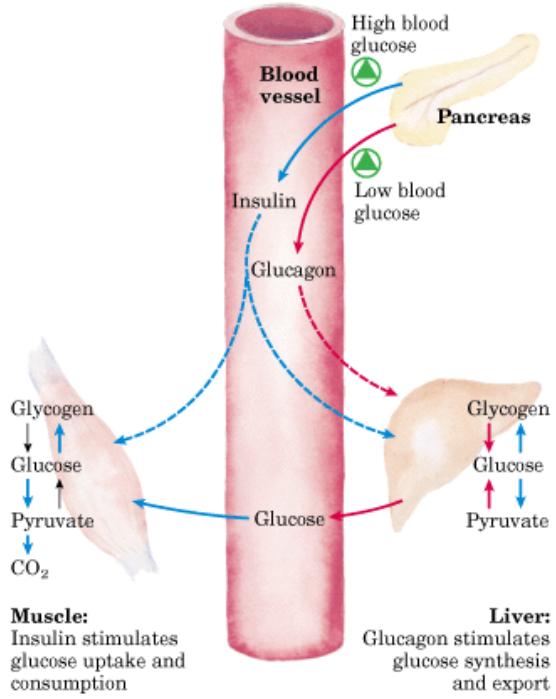

Pancreas
α cell (glucagon)
β cell (insulin)
Blood vessels
δ cell (somatostatin)


Preproinsulin
Proinsulin
Mature insulin
NH_3
Signal sequence
C
A
B
COO^-
S-S
A chain
B chain
H_3N
^-OOC
Signal sequence
C peptide

Diabetes mellitus

- Defecto en la producción o la acción de la insulina
- Tipo I (IDDM) o tipo II (NIDDM)
- Glicosuria: “excreción excesiva de orina dulce”
  - Poliuria y Polidipsia
- Excesiva pero incompleta oxidación de ácidos grasos
  - Cetosis, acidosis: cetoacidosis





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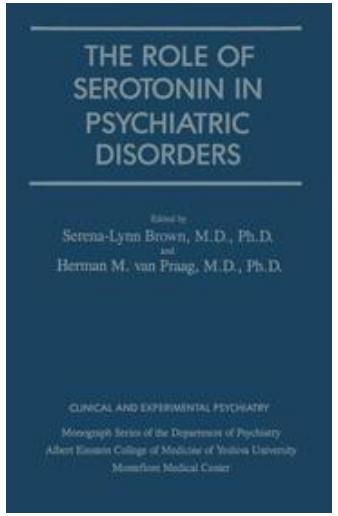
Aminoácidos y sus metabolitos como neurotransmisores y reguladores biológicos

- Glicina y glutamato
- GABA, producto de la descarboxilación del glutamato
- Histamina
- Serotonina, deriva del triptofano
- Catecolaminas (dopamina, adrenalina, noradrenalina) derivan de la tirosina



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Systematic review

Efficacy and safety of selective serotonin reuptake inhibitors in COVID-19 management: a systematic review and meta-analysis

Jiawen Deng [1,*], Daniel Rayner [2], Harikrishnaa B. Ramaraju [3], Umaima Abbas [4], Cristian Garcia [1], Kiyan Heybati [5], Fangwen Zhou [6], Emma Huang [7], Ye-Jean Park [1], Myron Moskalyk [6]

Association of serotonin reuptake inhibitors with asthma control.

- **Source:** Allergy & Asthma Proceedings . Sep2023, Vol. 44 Issue 5, p354-360. 7p.
- **Author(s):** Gajewski, Alexander J.; Palka, Jayme M.; Raitt, Josh M.; Agarwal, Catherine D.; Khan, David A.; Kao, Cindy H.; Brown, E. Sherwood

- **Abstract:** Background: Clinical trials demonstrated that selective serotonin reuptake inhibitors (SSRI) can improve asthma control in patients with comorbid major depressive disorder (MDD) and that this effect may be greater than the effect of SSRIs on depression. These findings suggest that SSRIs may improve asthma control in patients without MDD. Objective: The current retrospective study examined the effect of SSRIs and serotonin and norepinephrine reuptake inhibitors (SNRI) on asthma control in adult patients. We hypothesized that patients would have fewer asthma exacerbations after treatment with an SSRI or SNRI. Methods: Electronic health record data of adult patients (N = 592) who were seen at a University of Texas Southwestern (UTSW) hospital or clinic and had (1) an SSRI or SNRI prescription, (2) a previous asthma diagnosis, and (3) no mood disorder diagnosis were extracted by using the UTSW Clinical Data Exchange Network. Wilcoxon signed rank tests were used to compare oral corticosteroid prescriptions and asthma-related emergency department (ED) visits and hospitalizations in the 12 months before and after the start of an SSRI/SNRI. Results: Therapy with SSRIs/SNRIs was associated with a significant decrease in oral corticosteroid use (p = 0.003), ED visits (p = 0.002), and hospitalizations (p < 0.001). Conclusion: Results from the current study add to the existing literature by demonstrating a reduced rate of severe exacerbations in patients with asthma by using an SSRI/SNRI without limiting the analytic sample to a high-illness-severity subgroup defined by symptoms of asthma or depression. Future work should include a prospective, placebo controlled study with individuals who have asthma and no comorbid mental health condition, verified by a mental health professional.
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International Journal of *Molecular Sciences*

MDPI

Review

Cardiac Roles of Serotonin (5-HT) and 5-HT-Receptors in Health and Disease

Joachim Neumann [1,*], Britt Hofmann [2], Stefan Dhein [3] and Ulrich Gergs [1]

Open Access | Systematic Review

The Role of Serotonin in Fear Learning and Memory: A Systematic Review of Human Studies

by Francesco Tortora [1,†], Abed L. Hadipour [1], Simone Battaglia [2], Alessandra Falzone [1], Alessio Avenanti [2,3,*,‡] and Carmelo M. Vicario [1,*,‡]

Requires Authentication Published online by De Gruyter July 10, 2023

The brain serotonin system in autism

Alexander Ya Rodnyy, Elena M. Kondaurova, Anton S. Tsybko, Nina K. Popova, Dmitry A. Kudlay and Vladimir S. Naumenko

From the journal Reviews in the Neurosciences
https://doi.org/10.1515/revneuro-2023-0055

Dopamine
Endorphin
HAPPY HORMONES
Serotonin
Oxytocin

1

Vitamina D

7-Dehydrocholesterol

↓ UV light

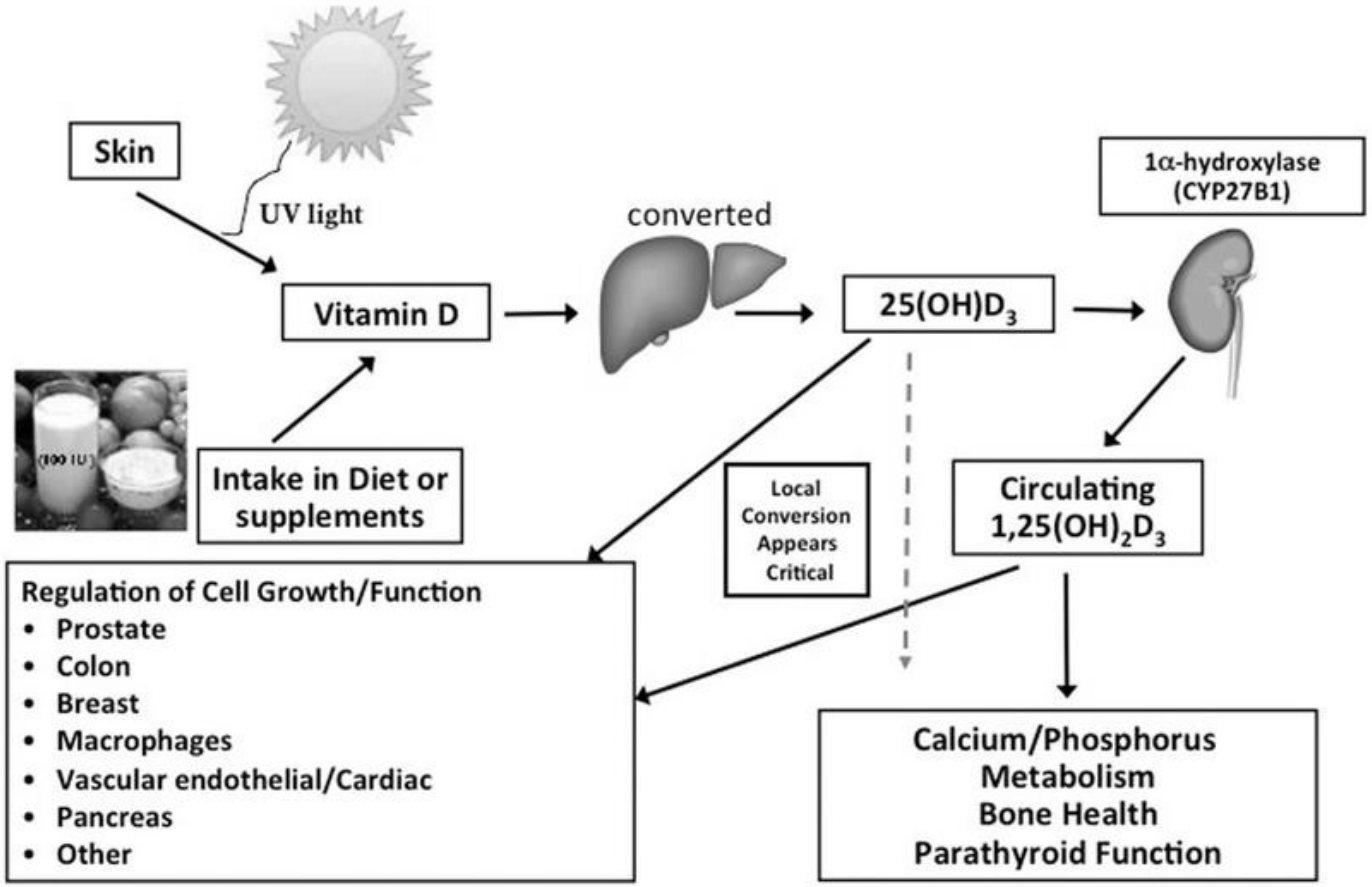
Vitamin D_3
(cholecalciferol)

↓

25-Hydroxycholecalciferol

↓

1,25-Dihydroxycholecalciferol



Retinoides

β-Carotene

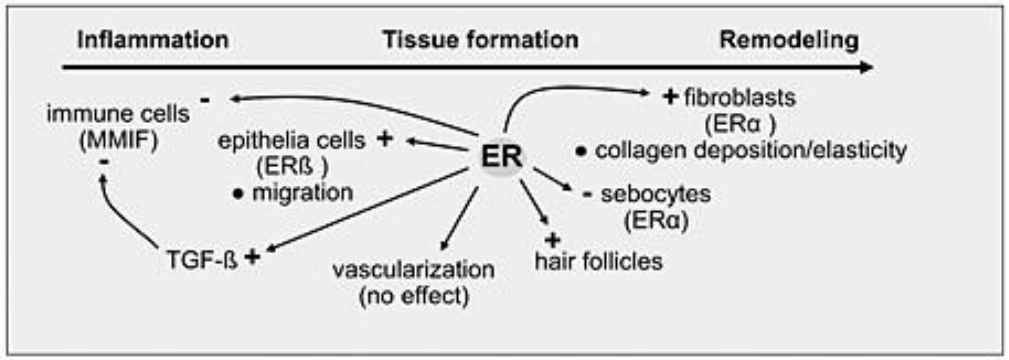
↓

Vitamin A_1
(retinol)

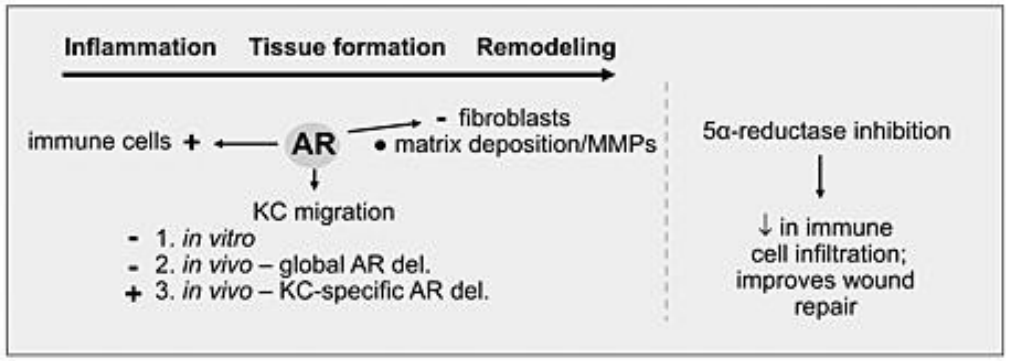
↓

Retinoic acid

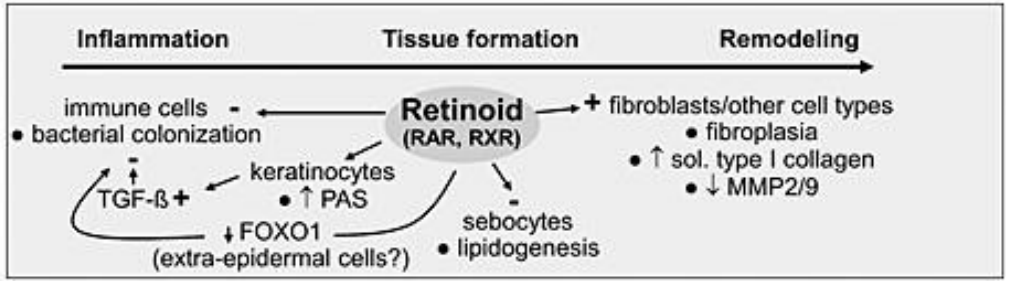
A. Estrogen receptor signaling



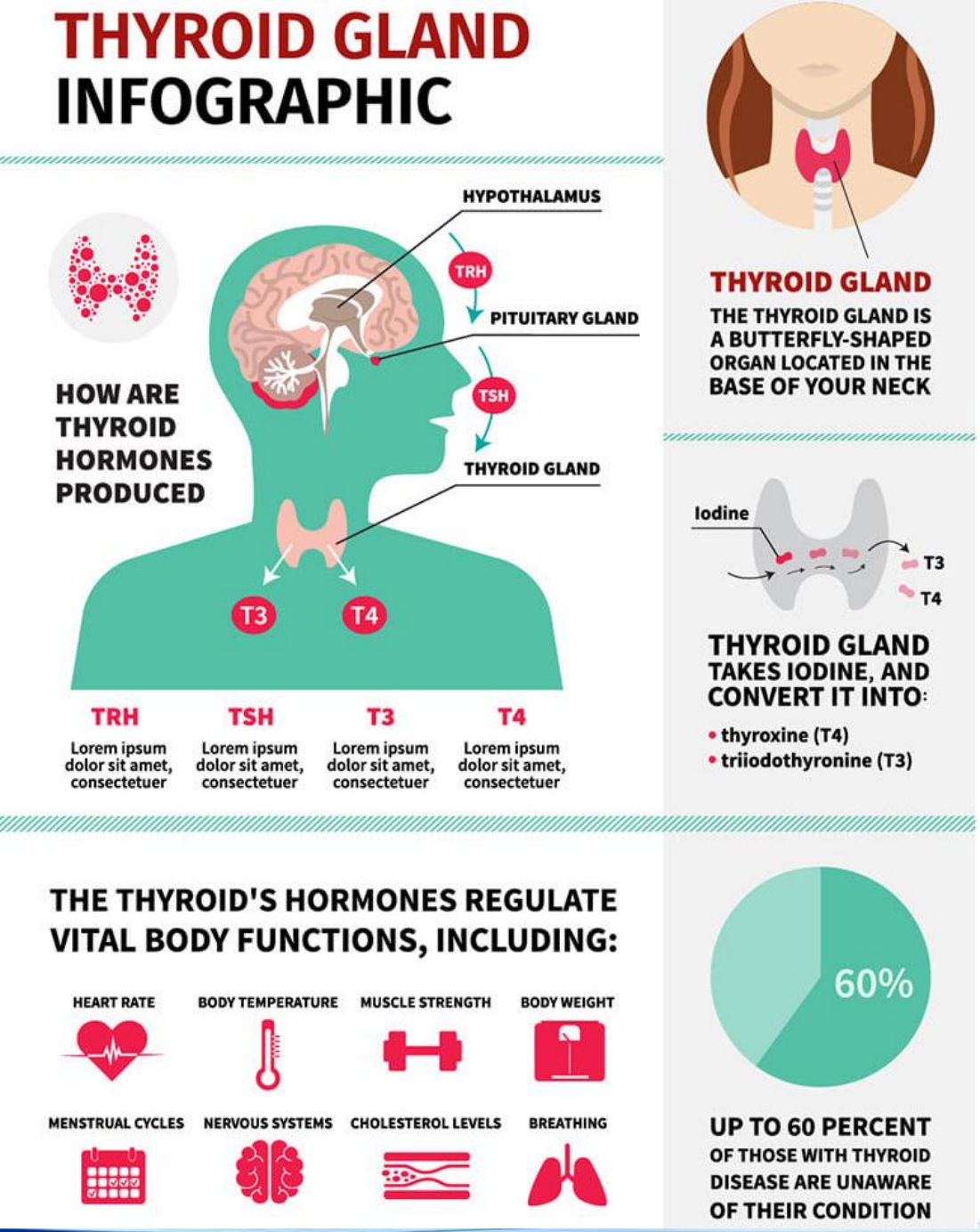
B. Androgen receptor signaling



C. Retinoid signaling



Hormonas tiroideas



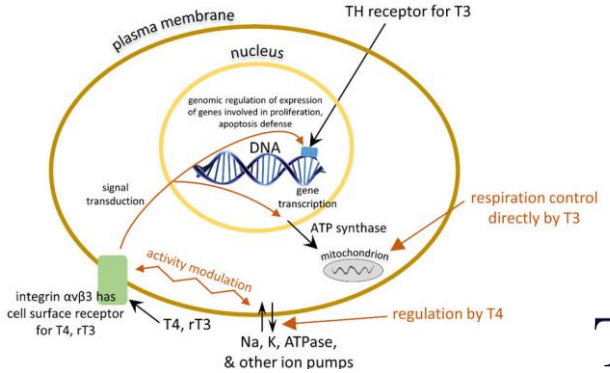
Thyroglobulin–Tyr

↓

Thyroglobulin–Tyr–I
(iodinated Tyr residues)

↓ proteolysis

Thyroxine (T_4)
and
triiodothyronine (T_3)



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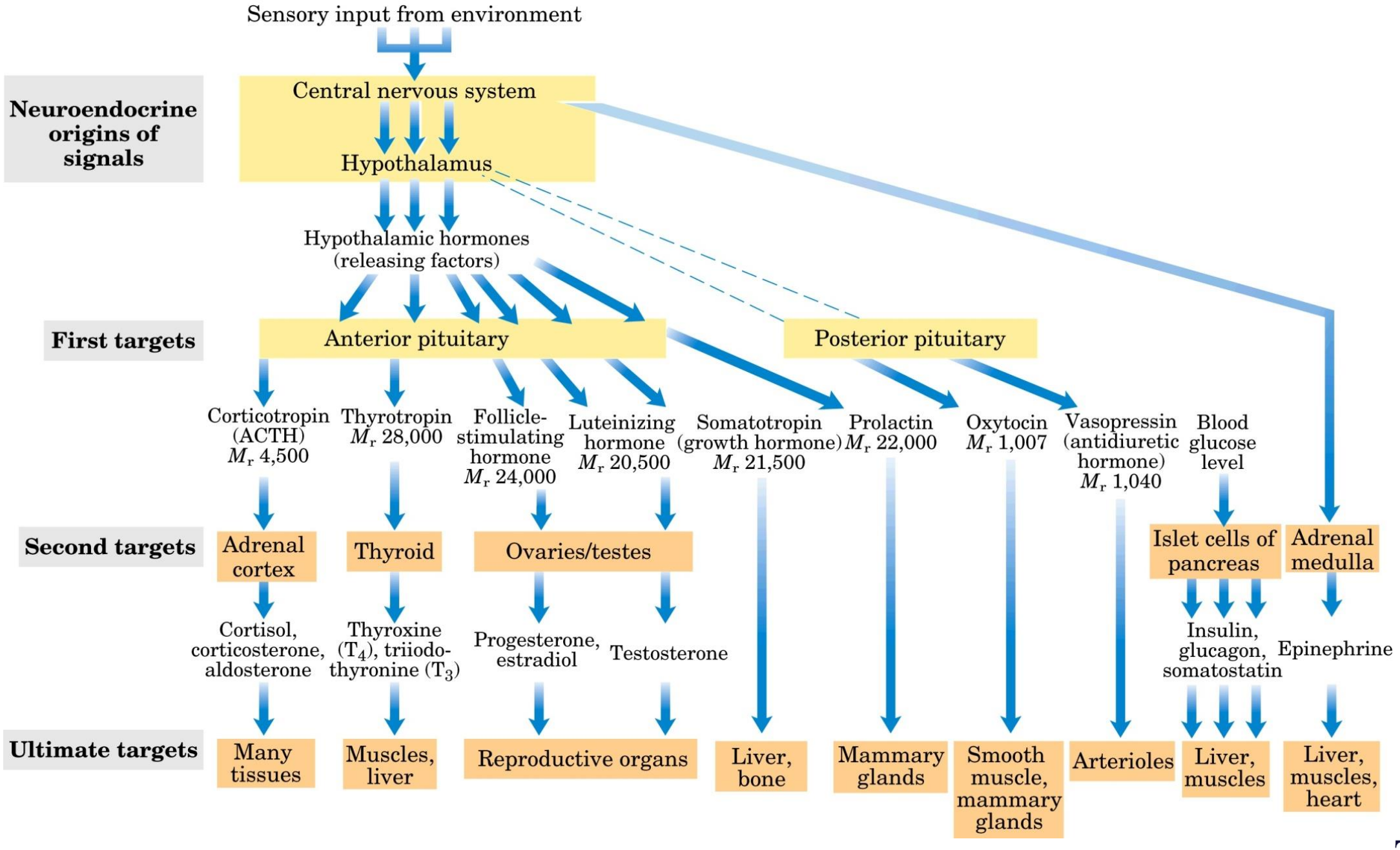
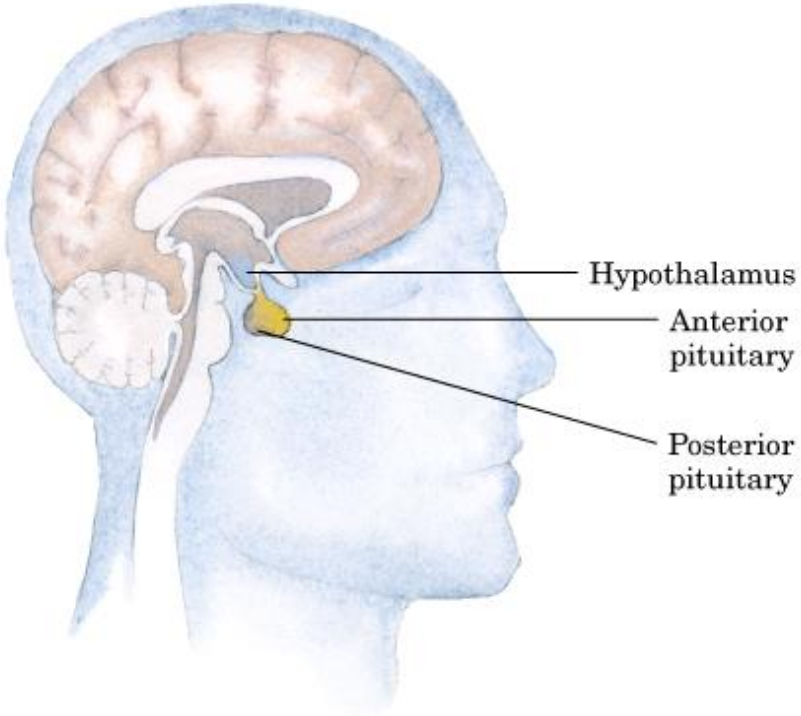
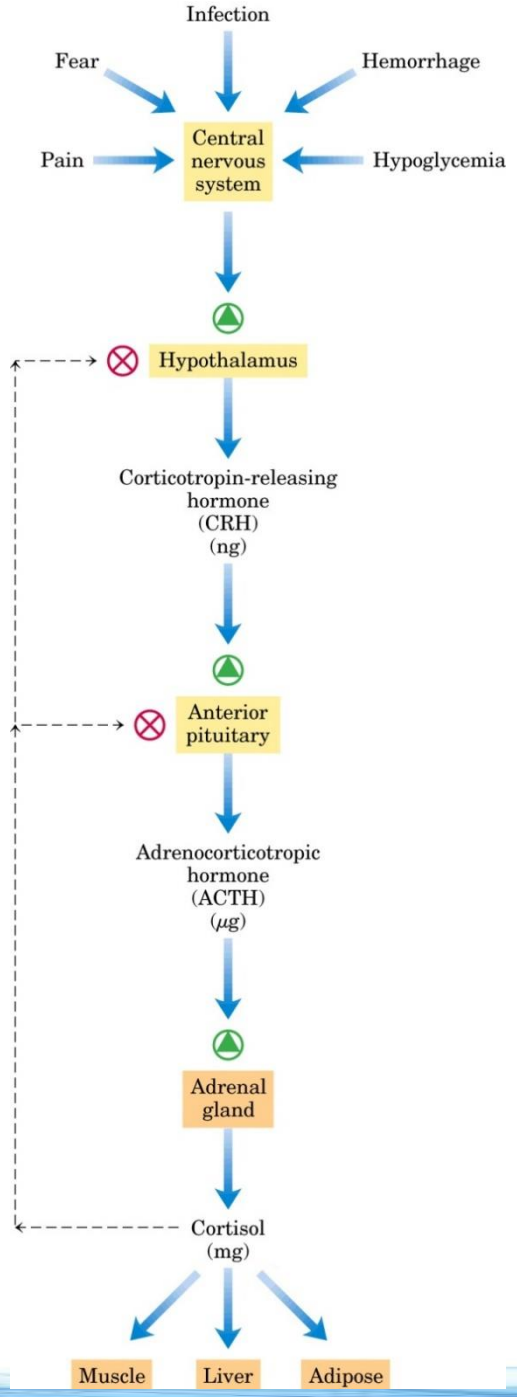
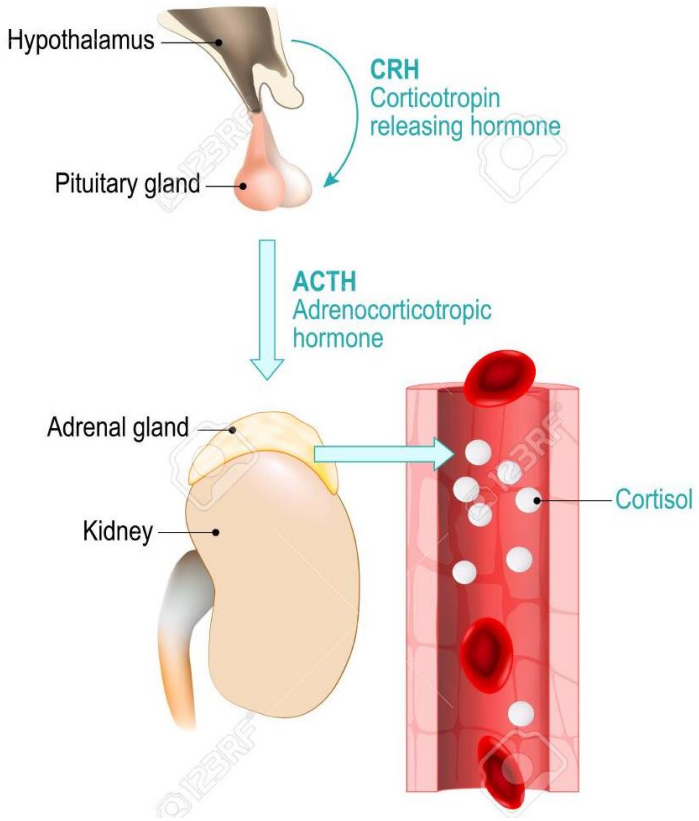

Sensory input from environment
Neuroendocrine origins of signals
Central nervous system
Hypothalamus
Hypothalamic hormones (releasing factors)
First targets
Anterior pituitary
Posterior pituitary
Corticotropin (ACTH) M_r 4,500
Thyrotropin M_r 28,000
Follicle-stimulating hormone M_r 24,000
Luteinizing hormone M_r 20,500
Somatotropin (growth hormone) M_r 21,500
Prolactin M_r 22,000
Oxytocin M_r 1,007
Vasopressin (antidiuretic hormone) M_r 1,040
Blood glucose level
Second targets
Adrenal cortex
Thyroid
Ovaries/testes
Islet cells of pancreas
Adrenal medulla
Cortisol, corticosterone, aldosterone
Thyroxine (T_4), triiodothyronine (T_3)
Progesterone, estradiol
Testosterone
Insulin, glucagon, somatostatin
Epinephrine
Ultimate targets
Many tissues
Muscles, liver
Reproductive organs
Liver, bone
Mammary glands
Smooth muscle, mammary glands
Arterioles
Liver, muscles
Liver, muscles, heart

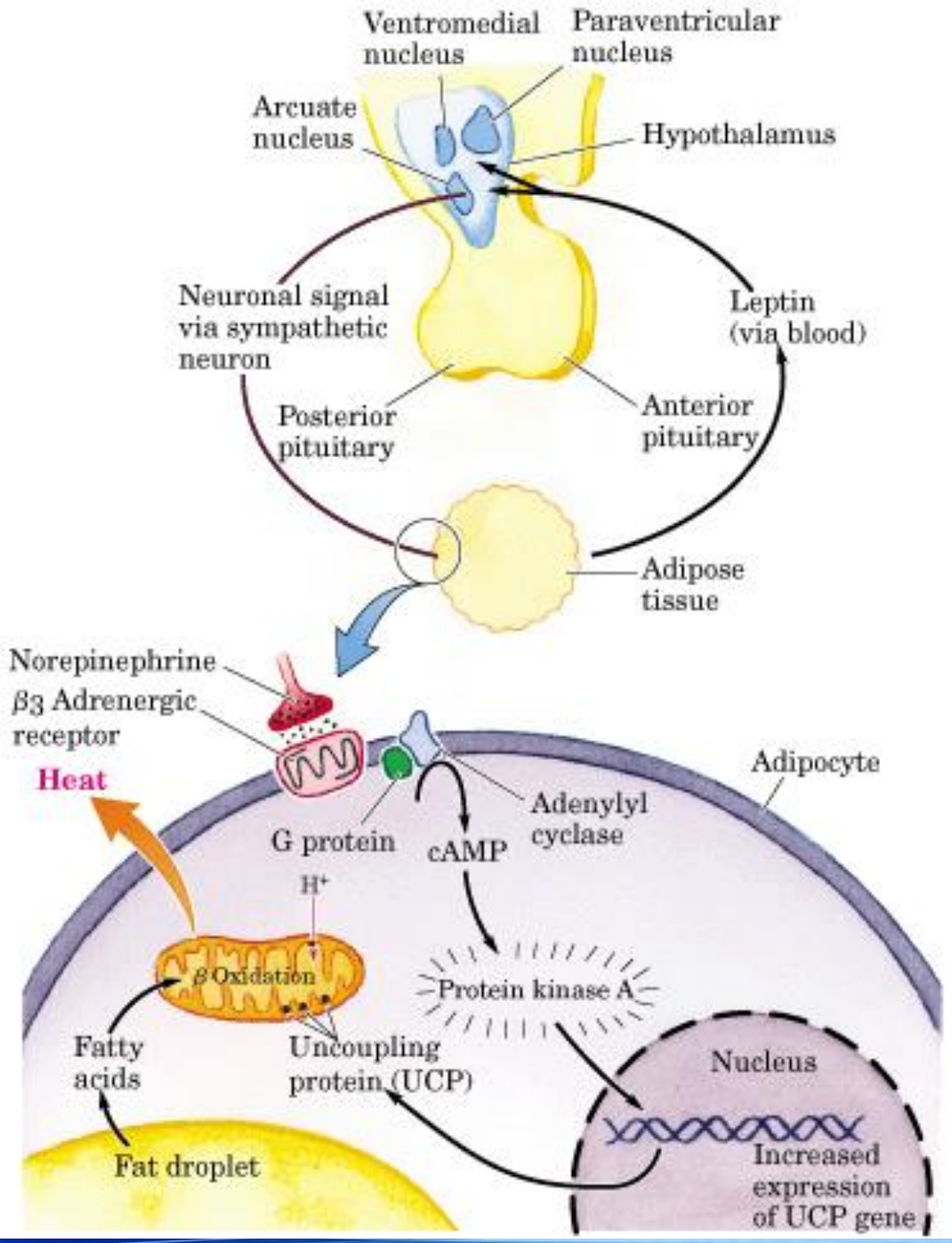
STRESS RESPONSE SYSTEM







Leptina / Grelina



frontiers | Frontiers in Endocrinology

The impact of leptin on sperm

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Handling Editor: Jessica Dunleavy

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Abstract

Despite its important role in numerous physiological functions, including regulation of appetite and body weight, immune function and normal sexual maturation, raised leptin levels could result in significant damaging effects on sperm. The adverse effects of leptin on the male reproductive system result from its direct actions on the reproductive organs and cells instead of the hypothalamus–pituitary–gonadal axis. Binding of leptin to the receptors in the seminiferous tubular cells of the testes increases free radical production and decreases the gene expression and activity of endogenous enzymatic antioxidants. These effects are mediated via the PI3K pathway. The resultant oxidative stress causes significant damage to the seminiferous tubular cells, germ cells and sperm DNA leading to apoptosis, increased sperm DNA fragmentation, decreased sperm count, increased fraction of sperm with abnormal morphology, and decreased seminiferous tubular height and diameter. This review summarises the evidence in the literature on the adverse effects of leptin on sperm, which could underlie the often-reported sperm abnormalities in obese hyperleptinaemic infertile males. Although leptin is necessary for normal reproductive function, its raised levels could be pathologic. There is, therefore, a need to identify the cut-off level in the serum and seminal fluid above which leptin becomes pathological for better management of leptin associated adverse effects on male reproductive function.

Check for updates

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SPECIALTY SECTION
This article was submitted to Clinical Diabetes, a section of the journal Frontiers in Endocrinology

Triglyc
recept
to pro
with ty

Hana Alzam

Department of Phy

Objectives: to
indices, and gl
compared to h

Methods: This
healthy control

nmunity 107 (2023) 53–61

ilable at ScienceDirect

or and Immunity

w.elsevier.com/locate/ybrbi

sease: Chronic inflammation,

[1], Hammad Yasin [d], Yining Zhao [e],
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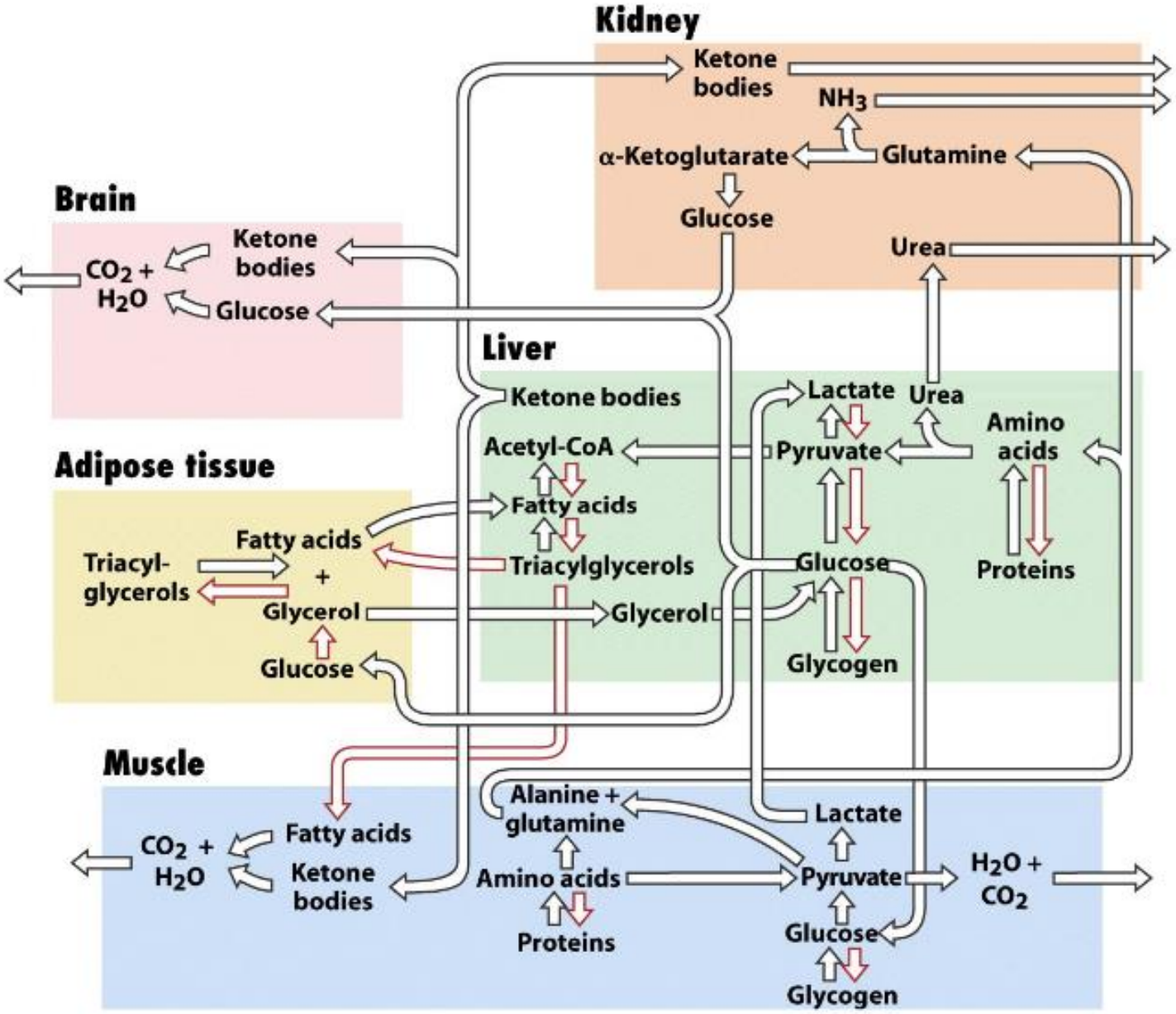
imental evidence implicates a relationship between immunometabolic deterioration
arkinson's disease (PD) with a dysregulation of central and peripheral neuro-
diated by circulating adipokines, in particular leptin. We screened the current liter-
ines in PD. Hence, we searched known databases (PubMed, MEDLINE/OVID) and
w articles using the following terms: "leptin/ObR", "Parkinson's disease", "immune-
and "neuroinflammation". Focusing on leptin, we summarize and discuss the existing

Efectos

- Anorexígenos ≠ Orexigénicos
- Hambre / Saciedad
- Motivación / Deseo
- Energía / Cansancio
- Alerta / Sueño
- Ansiedad / Satisfacción



Biohacks

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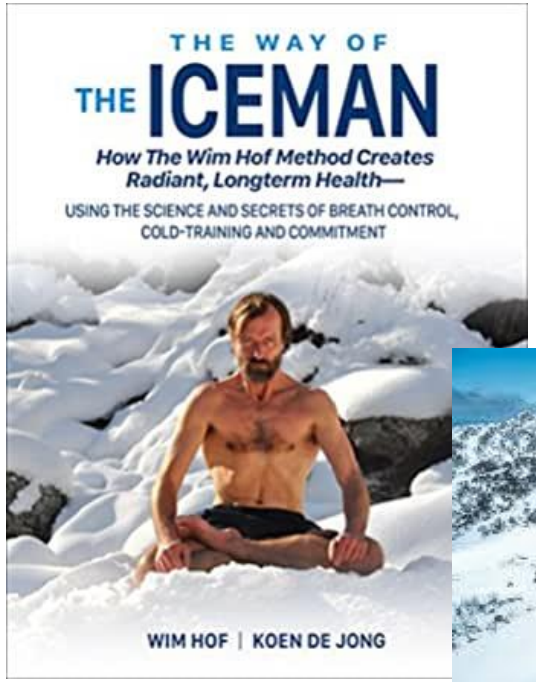
Biohacking (“pirateo corporal”)

- Nuestro cuerpo es un sistema
- Interactúa con sistemas
- Soluciones de bajo costo
- Efectivas
- Preventivas más que reparativas
- Optimizar cuerpo, mente, interacciones, etc

Método Wim-Hof



- Consiste en
  - Respiración,
  - Exposición al frío
  - Consistencia

- Algunos beneficios: fortalece el sistema inmune, aumenta la resistencia al frío, reduce el estrés, ayuda a controlar el peso, a dormir mejor, tener más energía, mejorar la concentración, regulación hormonal, etc…

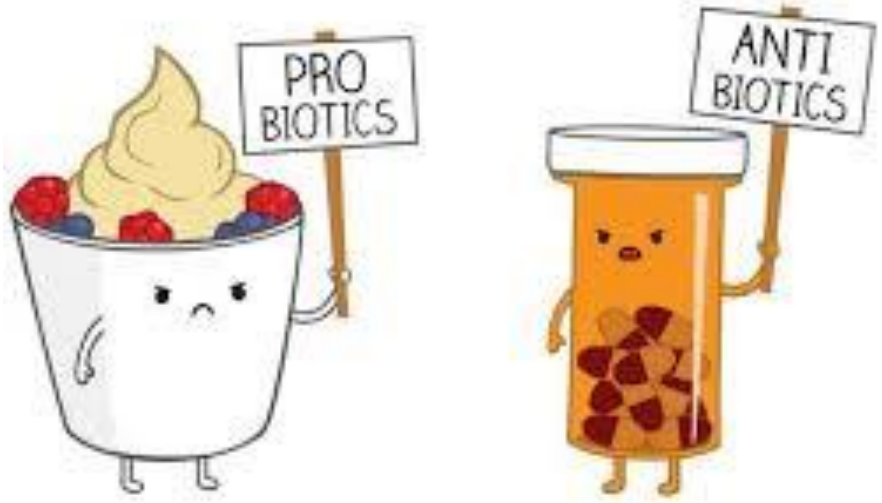
HIIT (*Entrenamiento con intervalos de alta intensidad*)

- Ayuda a perder peso
- Ayuda a generar músculo
- Mejora capacidad cardiopulmonar
- Promueve alternancia de estados anabólico y catabólico
- Promueve modificación hormonal, como la producción de testosterona

- Precauciones: duración de los intervalos

Fibra dietética

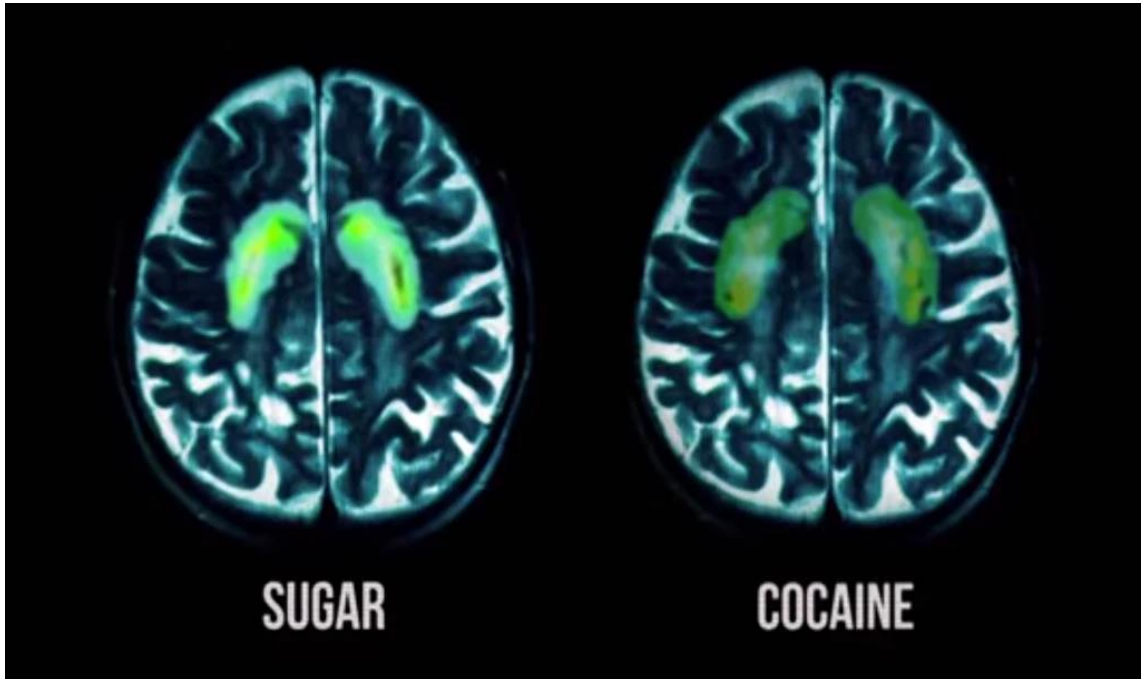
- Aumenta la excreción de ácidos biliares (Colesterol)
- Produce saciedad (aumenta el volumen fecal)
- Aumenta el tránsito intestinal (enlentece el vaciamiento gástrico)
- Actúa como prebiótico



Consumo carbohidratos

- Fomenta la disbiosis
- Fomenta un metabolismo anaerobio
- Aumento insulina
  - Interacción con hormona tiroides
  - Semejante a IGF-1(Insulin-like growth factor
  - Inflamación
  - Efecto adictivo
    - producción de serotonina, dopamina, …
- **Recomendación:**

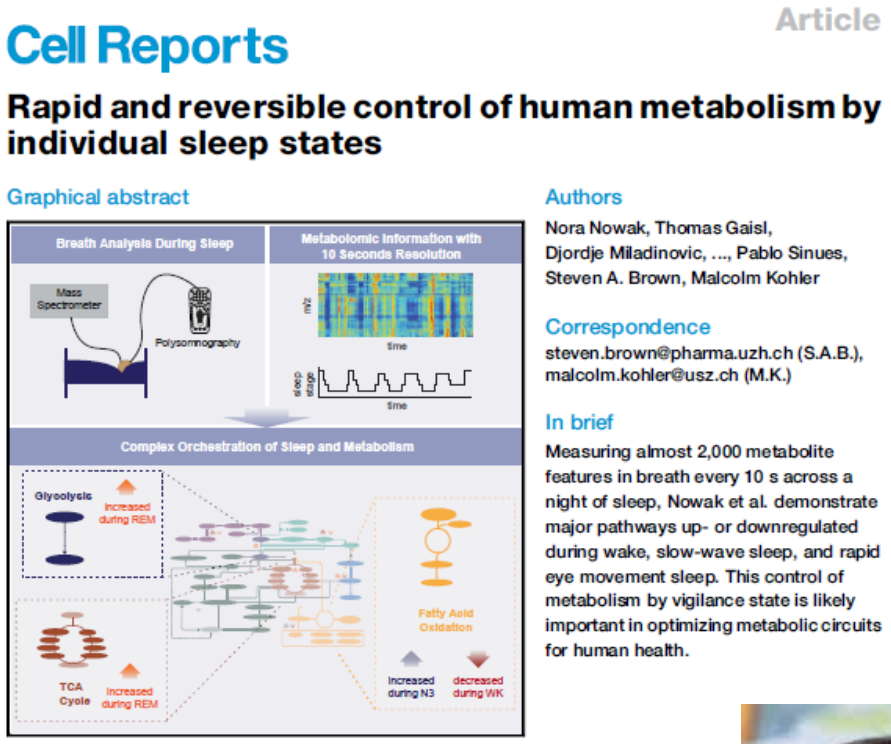
https://www.youtube.com/watch?v=OpM49NbKTP0



Fuente de la imagen: https://www.mic.com/articles/88015/what-happens-to-your-brain-on-sugar-explained-by-science

Para dormir

- **Opciones:**
  - Buena alimentación y ejercicio
  - Consumo de melatonina
  - Evitar luz de dispositivos electrónicos
  - Temperatura fresca
  - Regular la luz



Article

Cell Reports

Rapid and reversible control of human metabolism by individual sleep states

Graphical abstract

Authors

Nora Nowak, Thomas Gaisl, Djordje Miladinovic, ..., Pablo Sinues, Steven A. Brown, Malcolm Kohler

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steven.brown@pharma.uzh.ch (S.A.B.), malcolm.kohler@usz.ch (M.K.)

In brief

Measuring almost 2,000 metabolite features in breath every 10 s across a night of sleep, Nowak et al. demonstrate major pathways up- or downregulated during wake, slow-wave sleep, and rapid eye movement sleep. This control of metabolism by vigilance state is likely important in optimizing metabolic circuits for human health.

- **Beneficios:**
  - Regulación de algunas hormonas
  - Disminución del peso corporal
  - Remodelación cerebral y memoria a largo plazo
  - Regeneración del cuerpo
  - Menos enfermedades mentales

Dominar el propio cuerpo

- Propiocepción
  - Mejor equilibrio
  - Salud cardiovascular
  - Mayor agilidad
  - Mejor desarrollo cerebral
  - Estabilidad emocional

- Respiración
- Estiramientos (Yoga)
- “Pensamiento positivo”

Mindfulness

- Promueve
  - Neuroplasticidad
  - Propiocepción
  - Estabilidad emocional
    - Manejo del estrés
    - Regulación hormonal
    - Mejora del sueño

Ayuno intermitente

- Ayuda a
  - rotar (“renovar”) las reservas del cuerpo
  - evitar la permeabilidad intestinal
  - activar el metabolismo
  - bajar de peso
  - construir músculo
  - mejorar las defensas
  - “producir” células madre

Estrategias *preventivas* o *potenciadoras*

Acupuntura

Homeopatía

Ejercicio

Mindfulness

Baños de sol

Grupo social de apoyo

Propiocepción

Absortismo

Dieta apropiada

Ayuno